EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	112	"5512549"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2007/01/27 11:54
S1	5	Hathaway.IN. Baron.IN. Mistry.IN. Roman.IN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2007/01/27 11:53
S2	112	"5512549"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2007/01/26 19:06
S3	2	"20020107206"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2007/01/26 19:06

(FILE 'HOME' ENTERED AT 15:33:15 ON 24 JAN 2007)

```
FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 15:33:32 ON 24
            9302 S EXENDIN OR GLP-1 OR ("GLUCAGON-LIKE AGONIST")
           24309 S "FREE RADICAL SCAVENGER"
44707 S ISCHEM###### AND EVENT
          158841 S REPERFUSION
183126 S CARDIAC INTERVENTION OR (ANGIOPLASTY OR
"CORONARY BY PASS" OR
L6 110219 S CARDIAC AND (ISCHEMIA OR REPERFUSION OR
 "CONGESTIVE HEART FAI
            355 S METABOLIC INTERVENTION
74695 S ARRHYTHMIA AND (TREAT##### OR PREVENT#######)
L8
               4695 S ARRHYTHMA AND (TREAT##### OR I

4 S LI AND L8 AND PD<=20031219

I S LI AND L2 AND PD<=20031219

O S LI AND L3 AND PD<=20031219

O S LI AND L3 AND PD<=20031219

15 S LI AND L3 AND PD<=20031219

2 S LI AND L5 AND PD<=20031219

2 S LI AND L6 AND PD<=20031219

5 S LI AND L6 AND PD<=20031219

5 S LI AND L7 AND PD<=20031219

4 DUP REM L9 (0 DUPLICATES REMOVED)

5 DUP REM L13 (7 DUPLICATES REMOVED)
L10
LII
LI2
L13
L15
L17
                8 DUP REM L13 (7 DUPLICATES REMOVED)
2 DUP REM L14 (0 DUPLICATES REMOVED)
L19
 L20
                8 DUP REM L15 (0 DUPLICATES REMOVED)
4 DUP REM L16 (1 DUPLICATE REMOVED)
=> S Nephropathy OR ("END Stage renal disease") OR ESRD
L22 139696 NEPHROPATHY OR ("END STAGE RENAL DISEASE") OR ESRD
```

=> S Endothelial Function 22772 ENDOTHELIAL FUNCTION

=> S ProteinUria L24 82699 PROTEINURIA

L18

> S Glomerulosclerosi L25 21397 GLOMERULOSCLEROSIS

=> s Diabetes OR "Insulin resistance" OR hypertension

L26 1521989 DIABETES OR "INSULIN RESISTANCE" OR HYPERTENSION

=> S L1 AND L22 AND pd<=20031219

```
4 DUP REM L9 (0 DUPLICATES REMOVED)
8 DUP REM L13 (7 DUPLICATES REMOVED)
2 DUP REM L14 (0 DUPLICATES REMOVED)
8 DUP REM L15 (0 DUPLICATES REMOVED)
4 DUP REM L16 (1 DUPLICATE REMOVED)
139696 S NEPHROPATHY OR ("END STAGE RENAL DISEASE") OR ESRD
22772 S ENDOTHELIAL FUNCTION
82699 S PROTEINIBIA
  L21
L22
  1.23
                             82699 S PROTEINURIA
21397 S GLOMERULOSCLEROSIS
  L25
                         21397 S GLOMEROLOS-LEROSIS
1521989 S DIABETES OR "INSULIN RESISTANCE" OR HYPERTENSION
14 S L1 AND L22 AND PD=20031219
1 S L1 AND L23 AND PD<=20031219
1 S L1 AND L24 AND PD<=20031219
  L27
   L28
  L29
                                1 S L1 AND L25 AND PD<=20031219
1792 S L1 AND L26 AND PD<=20031219
  L30
  L31
  1.32
                                     13 S L31 AND L22
    => D Rem 127
  'REM' IS NOT A VALID FORMAT
  In a multifile environment, a format can only be used if it is valid
  in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
 or the STATGUIDE INCOMMENTATION OF COMMENTATION OF COMMENTATION OF COMMENTATION ALL FILES (FILEDEFAULT):
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT): Exit
'EXIT IS NOT A VALID FORMAT

TO STATE OF COMMENTATION ON THE PROPERTY OF COMMENTATION OF COM
  In a multifile environment, a format can only be used if it is valid
in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
  individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT): Dup Rem L27
 "DUP' IS NOT A VALID FORMAT
"REM' IS NOT A VALID FORMAT
"L115' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
  in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in
  individual files.
 REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):0
'0' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files. Refer to file specific help messages
 or the STNGUIDE file for information on formats available in
 individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT): Ibib
```

```
14 L1 AND L22 AND PD<=20031219
   S L1 AND L23 AND pd<=20031219
  3 FILES SEARCHED.
           1 L1 AND L23 AND PD<=20031219
=> S L1 AND L24 AND pd<=20031219
3 FILES SEARCHED...
          1 L1 AND L24 AND PD<=20031219
=> $ L1 AND L25 AND pd<=20031219
   3 FILES SEARCHED
           1 LI AND L25 AND PD<=20031219
=> S L1 AND L26 AND pd<=20031219
  3 FILES SEARCHED...
31 1792 L1 AND L26 AND PD<=20031219
L31
  > S L31 AND L22
L32
        13 L31 AND L22
=> D Hist
   (FILE 'HOME' ENTERED AT 15:33:15 ON 24 JAN 2007)
   FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 15:33:32 ON 24
         9302 S EXENDIN OR GLP-1 OR ("GLUCAGON-LIKE AGONIST")
        24309 S "FREE RADICAL SCAVENGER"
44707 S ISCHEM###### AND EVENT
        158841 S REPERFUSION
138841 S. REPERFUSION

138841 S. CARDIAC INTERVENTION OR (ANGIOPLASTY OR
"CORONARY BY PASS" OR
110219 S. CARDIAC AND (ISCHEMIA OR REPERFUSION OR
"CONGESTIVE HEART FAI
        183126 S CARDIAC INTERVENTION OR (ANGIOPLASTY OR
         355 S METABOLIC INTERVENTION
74695 S ARRHYTHMIA AND (TREAT##### OR PREVENT#######)
          4993 3 ARRHT I HMIA AND (IREA 11#4

4 S LI AND L8 AND PD<=20031219

1 S LI AND L2 AND PD<=20031219

0 S LI AND L3 AND PD<=20031219

15 S LI AND L3 AND PD<=20031219

15 S LI AND L4 AND PD<=20031219
L13
            2 S L1 AND L5 AND PD<=20031219
8 S L1 AND L6 AND PD<=20031219
L15
            5 S L1 AND L7 AND PD<=20031219
```

3 FILES SEARCHED.

```
L27 ANSWER I OF 14 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
 ACCESSION NUMBER: 2003:390202 BIOSIS <<LOGINID::20070124>> DOCUMENT NUMBER: PREV200300390202
                           The glucagon-like peptides: A double-edged therapeutic
                     sword?.
AUTHOR(S): Perry, TracyAnn [Reprint Author]; Greig, Nigel H.
CORPORATE SOURCE: Section of Drug Design and Development, Laboratory of
Neurosciences, Gerontology Research Center, National
Institute on Aging, National Institutes of Health, 5600
Nathan Shock Drive, Baltimore, MD, 21224, USA
Natinat Shock Drive, Battimore, MD, 21224, USA
perty@gre.nia.nib.gov

SOURCE: Trends in Pharmacological Sciences, (July 2003)
Vol. 24, No. 7, pp. 377-383. print.
ISSN: 0165-6147 (ISSN print).

DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE:
                               English
Entered STN: 27 Aug 2003
 ENTRY DATE:
                     Last Updated on STN: 27 Aug 2003
=> Dup Rem 127
PROCESSING COMPLETED FOR L27
```

9 DUP REM L27 (5 DUPLICATES REMOVED) => Dup Rem 132 PROCESSING COMPLETED FOR L32 L34 9 DUP REM L32 (4 DUPLICATES REMOVED)

=> D Ibib All L28

L28 ANSWER I OF I CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2003:447519 CAPLUS <<LOGINID::20070124>> DOCUMENT NUMBER: 139:255595 Antihypertensive effect of glucagon-like peptide 1 in

Dahl salt-sensitive rats Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly, Annette; Ditter, Katie; Mistry, Mahesh; Roman, Richard AUTHOR(S):

SOURCE: Department of Physiology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA CORPORATE SOURCE: Journal of Hypertension (2003), 21(6), 1125-1135 SOURCE:

CODEN: JOHYD3; ISSN: 0263-6352

PUBLISHER: Lippincott Williams & Wilkins

```
LANGUAGE: English
AN 2003:447519 CAPLUS << LOGINID::20070124>>
 DN 139:255595
 ED Entered STN: 11 Jun 2003
 TI Antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive
AU Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly, Annette; Ditter,
Katie; Mistry, Mahesh; Roman, Richard J.
CS Department of Physiology, Medical College of Wisconsin, Milwaukee, WI,
SO Journal of Hypertension (2003), 21(6), 1125-1135
CODEN: JOHYD3; ISSN: 0263-6352
PB Lippincott Williams & Wilkins
DT Journal
LA English
 CC 2-6 (Mammalian Hormones)
AB Dahl salt-sensitive (Dahl S) rats exhibit many phenotypic traits associated
         with salt-sensitive hypertension in man. Specifically, they are salt-sensitive, insulin-resistant and hyperlipidemic. They also develop endothelial dysfunction, cardiac injury and glomeruloselerosis. Insulin resistance is linked to hypertension, renal and cardiac damage and
         restance is linked to hypertension, renal and cardiac damage and endothelial dysfunction. Thus, an agent that has diuretic action and can improve insulin resistance, like recombinant glucagon-like peptide-1(7-36)amide (rGLP-1), may have an antihypertensive effect. To determine whether chronic administration of rGLP-1 attenuates the developr of hypertension, endothelial dysfunction and/or hypertension-induced renal
       of hypertension, endothelial dysfunction and/or hypertension-induced renal and cardiac end organ damage in Dahl S rats. Mean arterial pressure (MAP) and urinary excretion of protein and albumin were measured in Dahl S rats before and after they were fed a 8% NaCl diet and infused with rGLP-1 (1 mg/kg per min, i.v.) or whicle for 14 days. At the end of the study, the degree of renal and cardiac injury was histol. assessed and endothelium-dependent relaxing function was studied using aortic rings. In other rats, the effects of rGLP-1 on sodium and water balance and plasma glucose and insulin levels for the first 3 days following a step change in sodium intake from a 0.1% NaCl diet to 7.5 mEq/day were determined The rGLP-1 significantly attenuated the development of hypertension in Dahl S rats (136 vs. 174 mmHg). This was associated with reduction in proteinuria (46 vs. 128 mg/day) and buminuria (46 vs. 86 mg/day) and
        Dahl S rats (136 vs. 174 mmHg). This was associated with reduction in proteinuria (46 vs. 128 mg/day) and albuminuria (46 vs. 86 mg/day) and improvement of endothelial function and renal and cardiac damage. The rGLP-1 markedly increased urine flow and sodium excretion for the first 3 days following elevation in sodium intake. It had no significant effects on plasma glucose and insulin conens. The rGLP-1 has antihypertensive and cardiac and renoprotective effects in Dahl S rats fed a high salt diet. The antihypertensive effect of rGLP-1 in
```

Dahl S rats is due mainly to its diuretic and natriuretic effects, rather

DOCUMENT TYPE:

Journal

```
RL: BSU (Biological study, unclassified); BIOL (Biological study)
                            (GLP-1 effect on water and sodium excretion in Dahl
                              salt-sensitive hypertensive rats)
       IT 89750-14-1, Glucagon-like peptide 1 118549-37-4, Insulinotropin
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
                    (Biological study); USES (Uses)
(antihypertensive effect of glucagon-like peptide 1 in Dahl
        RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS
       RECORD
RE
(1) Anderson, S; J Clin Invest 1985, V76, P612 CAPLUS
(2) Barragan, J; Am J Physiol 1994, V266, PE459 CAPLUS
(3) Bishop, J; Cardiovasc Res 2000, V47, P57 CAPLUS
(4) Bullock, B; Endocrinology 1996, V137, P2968 CAPLUS
(5) Campesc, V; Hypertension 1994, V23, P531 MEDLINE
(6) Dall'Aglio, E; Am J Hypertens 1991, V4, P773 CAPLUS
(7) DeFronzo, R; J Clin Invest 1976, V58, P83 CAPLUS
(8) DeFronzo, R; J Clin Invest 1976, V58, P83 CAPLUS
(9) Dengel, D; Hypertension 1996, V28, P127 MEDLINE
(10) Epstein, M; Hypertension 1996, V28, P127 MEDLINE
(11) Eprannini, E; N Engl J Med 1987, V317, P350 MEDLINE
(12) Greene, A; Am J Physiol 1990, V258, PH508 MEDLINE
(13) Grin, C; Hypertension 1990, V35, P803 MEDLINE
(14) Hayakawa, H; Circulation 1997, V96, P2407 CAPLUS
(15) Ito, O; Hypertension 1999, V33, P419 CAPLUS
(15) Ito, O; Hypertension 1999, V375, PR788 CAPLUS
(17) Kim, S; Br J Pharm 1996, V118, P549 CAPLUS
(18) Kotchen, T; Am J Hypertens 1997, V10, P1020 CAPLUS
(19) Kotchen, T; Am J Hypertens 1997, V10, P1020 CAPLUS
(20) Miller, A; J Cardiovasc Pharm Ther 1998, V3, P125 CAPLUS
(21) Minireview, D; Endocrinology 2001, V142, P521
(22) Mogensen, C; Scand J Clin Lab Invest 1976, V36, P383 MEDLINE
(23) Mondon, C; Metabolism 1988, V37, P303 CAPLUS
(24) Morron, C; Eur J Pharm 2002, V434, P163 CAPLUS
(25) Nauck, M; Exp Clin Endocrinol Diabetes 1997, V105, P187 CAPLUS
(26) Orskov, C; Diabetes 1994, V43, P535 CAPLUS
(27) O'Bryan, G; Semin Nephrol 1997, V17, P93 CAPLUS
(28) Parving, H; Lancet 1983, V1, P1175 MEDLINE
(31) Rawen, G; Hypertension 1982, V4, P753 MEDLINE
(31) Rawen, G; Hypertension 1982, V4, P753 MEDLINE
(32) Righ, J; Hypertension 1992, V45, P111 MEDLINE
(33) Roman, R; Am J Hypertens 1997, V10, P63S CAPLUS
(34) Sakamoto, S; Diabetes 1998, V47, P82 CAPLUS
       (1) Anderson, S; J Clin Invest 1985, V76, P612 CAPLUS
```

```
ST hypertension GLP1; sodium water excretion hypertension GLP1; glucose insulin blood hypertension GLP1; aorta heart kidney damage hypertension
   GLP1; albuminuria proteinuria hypertension GLP1; antihypertensive GLP1
    diuresis natriuresis
    Hypertension
(Dahl salt-sensitive; antihypertensive effect of glucagon-like peptide
l in Dahl salt-sensitive rats)
IT Heart, disease
   Kidney, disease
(GLP-1 effect on aorta endothelium and heart and
       kidney damage in Dahl salt-sensitive hypertensive rats)
IT Blood pressure
   Heart rate
      (GLP-1 effect on blood pressure and heart rate in
Dahl salt-sensitive hypertensive rats)
IT Albumins, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(albuminuria; GLP-1 effect on albuminuria and
      proteinuria in Dahl salt-sensitive hypertensive rats)
IT Antihypertensives
      (antihypertensive action of GLP-1 in Dahl
       salt-sensitive hypertensive rats is due to diuretic and natriuretic
       actions)
    Artery, disease
      (aortic endothelial injury; GLP-1 effect on aorta
endothelium and heart and kidney damage in Dahl salt-sensitive
      hypertensive rats)
      (aortic endothelial; GLP-1 effect on aorta
       endothelium and heart and kidney damage in Dahl salt-sensitive
      hypertensive rats)
      (aortic, disease, injury; GLP-1 effect on aorta endothelium and heart and kidney damage in Dahl salt-sensitive
      hypertensive rats)
   RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteinuria; GLP-1 effect on albuminuria and
proteinuria in Dahl salt-sensitive hypertensive rats)

T 50-99-7, Glucose, biological studies 9004-10-8, Insulin, biological
   studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
      (GLP-1 effect on blood glucose and insulin in Dahl salt-sensitive hypertensive rats)
IT 7440-23-5, Sodium, biological studies 7732-18-5, Water, biological
```

than an effect to improve insulin-resistance.

```
(35) Salonen, J. Diabetes 1998, V47, P270 CAPLUS
(36) Shimabukuro, M. Metabolism 1996, V45, P1168 CAPLUS
(37) Sterzel, R.; Kidney Int 1988, V33, P1119 MEDLINE
(38) Tierney, W.; Am J Kidney Dis 1989, V13, P485 MEDLINE
(39) Tobian, L.; Hypertension 1979, V1, P316 CAPLUS
(40) Toft-Nielsen, M.; Diabetes Care 1999, V22, P1137 MEDLINE
(41) Vella, A.; Diabetes 2000, V49, P611 CAPLUS
(42) Yagi, K.; Hypertension 1997, V29, P728 CAPLUS
(43) Yamamoto, H.; J Clin Invest 2002, V110, P43 CAPLUS
(44) Zou, A.; Hypertension 1996, V27, P631 CAPLUS
 => D Ibib ALL 128
 L28 ANSWER I OF I CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:447519 CAPLUS <<LOGINID::20070124>>
DOCUMENT NUMBER: 139:255595
                                   Antihypertensive effect of glucagon-like peptide I in
                            Dahl salt-sensitive rats
Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly,
 AUTHOR(S):
                            Annette; Ditter, Katie; Mistry, Mahesh; Roman, Richard
                             SOURCE: Department of Physiology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA
 CORPORATE SOURCE:
 SOURCE:
                                       Journal of Hypertension (2003), 21(6),
                           1125-1135
CODEN: JOHYD3; ISSN: 0263-6352
 PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
DOCUMENT TYPE: Journal
LANGUAGE: English
AN 2003:447519 CAPLUS <<LOGINID::20070124>>
DN 139:255595
ED Entered STN: 11 Jun 2003
 TI Antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive
rats
AU Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly, Annette; Ditter,
Katie; Mistry, Mahesh; Roman, Richard J.
CS Department of Physiology, Medical College of Wisconsin, Milwaukee, WI,
     53226, USA
 SOJ Journal of Hypertension (2003), 21(6), 1125-1135
CODEN: JOHYD3; ISSN: 0263-6352
PB Lippincott Williams & Wilkins
 PB Lippince
DT Journal
LA English
CC 2-6 (Mammalian Hormones)
        Dahl salt-sensitive (Dahl S) rats exhibit many phenotypic traits associated
```

with salt-sensitive hypertension in man. Specifically, they are salt-sensitive, insulin-resistant and hyperlipidemic. They also develop endothelial dysfunction, cardiac injury and glomenuloselerosis. Insulin resistance is linked to hypertension, renal and cardiac damage and endothelial dysfunction. Thus, an agent that has diuretic action and can improve insulin resistance, like recombinant glucagon-like peptide-1(7-36)amide (rGLP-1), may have an antihypertensive effect. To peptide-1(7-36)amide (rGLP-1), may have an antihypertensive effect. To determine whether chronic administration of rGLP-1 attenuates the development of hypertension, endothelial dysfunction and/or hypertension-induced renal and cardiac end organ damage in Dahl S rats. Mean arterial pressure (MAP) and urinary excretion of protein and albumin were measured in Dahl S rats before and after they were fed a 8% NaCl diet and infused with rGLP-1 (1 mg/kg per min, i.v.) or vehicle for 14 days. At the end of the study, the degree of renal and cardiac injury was histol. assessed and endothelium-dependent relaxing function was studied using sortic rings. In other rats, the effects of rGLP-1 on sodium and water balance and lastma places and inclined levels for the first 3 days following a step plasma glucose and insulin levels for the first 3 days following a step change in sodium intake from a 0.1% NaCl diet to 7.5 mEq/day were determined change in sodium intake from a 0.1% NaCl diet to 7.5 mEq/day were dete The rGLP-1 significantly attenuated the development of hypertension in Dahl S rats (136 vs. 174 mmHg). This was associated with reduction in proteinuria (46 vs. 128 mg/day) and albuminuria (46 vs. 86 mg/day) and improvement of endothelial function and renal and cardiac damage. The rGLP-1 markedly increased urine flow and sodium excretion for the first 3 days following elevation in sodium intake. It had no significant effects on plasma glucose and insulin concers. The rGLP-1 has antihypertensive and cardiac and renoprotective effects in Dahl S rats fed a high salt diet. The antihypertensive effect of rGLP-1 in Dahl S rats is due mainly to its diuretic and natriuretic effects, rather than an effect to improve insulin-resistance.

ST hypertension GLP1; sodium water excretion hypertension GLP1; glucose insulin blood hypertension GLP1; aorta heart kidney damage hypertension GLP1; albuminuria proteinuria hypertension GLP1; antihypertensive GLP1

IT Hypertension

(Dahl salt-sensitive; antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive rats)

IT Heart, disease

Kidney, disease

(GLP-1 effect on aorta endothelium and heart and

kidney damage in Dahl salt-sensitive hypertensive rats) IT Blood pressure

(GLP-I effect on blood pressure and heart rate in

Dahl salt-sensitive hypertensive rats)
IT Albumins, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

```
(7) DeFronzo, R; Diabetologia 1981, V21, P165 CAPLUS
(8) DeFronzo, R; J Clin Invest 1976, V58, P83 CAPLUS
(9) Dengel, D; Hypertension 1996, V28, P127 MEDLINE
(10) Epstein, M; Hypertension 1996, V28, P127 MEDLINE
(11) Ferrannini, E; N Engl J Med 1987, V317, P350 MEDLINE
(12) Greene, A; Am J Physiol 1990, V258, PH508 MEDLINE
(13) Grim, C; Hypertension 1999, V35, P803 MEDLINE
(14) Hayakawa, H; Circulation 1997, V96, P2407 CAPLUS
(15) Ito, O; Hypertension 1999, V33, P419 CAPLUS
(16) Katakam, P; Am J Physiol 1998, V275, PR788 CAPLUS
(17) Kim, S; Br J Pharm 1996, V118, P549 CAPLUS
(18) Kotchen, T; Am J Hypertens 1997, V10, P1020 CAPLUS
(19) Kotchen, T; Am J Physiol 1991, V261, P2692 CAPLUS
(10) Miller, A; J Cardiovasc Pharm Ther 1998, V3, P125 CAPLUS
(21) Minireview, D; Endocrinology 2001, V142, P521
(22) Mogensen, C; Scand J Clin Lab Invest 1976, V36, P333 MEDLINE
(23) Mondon, C; Metabolism 1988, V37, P303 CAPLUS
(24) Moreno, C; Eur J Pharm 2002, V434, P163 CAPLUS
(25) Nauck, M; Exp Clin Endocrinol Diabetes 1997, V105, P187 CAPLUS
(26) Orskov, C; Diabetes 1994, V43, P335 CAPLUS
(27) O'Bryan, G; Semin Nephrol 1997, V17, P93 CAPLUS
(28) Parving, H; Lancet 1983, V1, P1175 MEDLINE
(29) Raij, L; Am J Med 1985, V79, P37 CAPLUS
(30) Rapp, J; Hypertension 1982, V4, P753 MEDLINE
(31) Raevan, G; Hypertension 1999, V245, P111 MEDLINE
(32) Ritz, E; J Intem Med 1999, V245, P111 MEDLINE
(33) Roman, R; Am J Hypertens 1997, V10, P635 CAPLUS
(34) Sakamoto, S; Diabetes 1998, V47, P270 CAPLUS
(35) Salonen, J; Diabetes 1998, V47, P270 CAPLUS
(36) Shimabukuro, M; Metabolism 1996, V45, P1168 CAPLUS

(35) Salonen, J. Diabetes 1998, V47, P270 CAPLUS
(36) Shimabukuro, M.; Metabolism 1996, V45, P1168 CAPLUS
(37) Sterzel, R.; Kidney Int 1988, V33, P1119 MEDLINE
(38) Tierney, W.; Am J Kidney Dis 1989, V13, P485 MEDLINE
(39) Tobian, L.; Hypertension 1979, V1, P316 CAPLUS
(40) Toft-Nielsen, M.; Diabetes Care 1999, V22, P1137 MEDLINE
(41) Vella, A.; Diabetes 2000, V49, P611 CAPLUS
(42) Yagi, K.; Hypertension 1997, V29, P728 CAPLUS
(43) Yamamoto, H.; J Clin Invest 2002, V110, P43 CAPLUS
(44) Zou, A.; Hypertension 1996, V27, P631 CAPLUS
```

≈> D (bib all 129

L29 ANSWER I OF I CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: DOCUMENT NUMBER: 2003:447519 CAPLUS <<LOGINID::20070124>> 139:255595 Antihypertensive effect of glucagon-like peptide 1 in

(albuminuria: GLP-1 effect on albuminuria and proteinuria in Dahl salt-sensitive hypertensive rats)
IT Antihypertensives (antihypertensive action of GLP-1 in Dahl salt-sensitive hypertensive rats is due to diuretic and natriuretic actions) IT Artery, disease (aortic endothelial injury; GLP-1 effect on aorta endothelium and heart and kidney damage in Dahl salt-sensitive hypertensive rats) (aortic endothelial: GLP-1 effect on aorta endothelium and heart and kidney damage in Dahl salt-sensitive hypertensive rats) IT Endothelium
(aortic, disease, injury; GLP-1 effect on aorta endothelium and heart and kidney damage in Dahl salt-sensitive hypertensive rats) RL: BSU (Biological study, unclassified); BIOL (Biological study) (proteinuria; GLP-1 effect on albuminuria and proteinuria in Dahl salt-sensitive hypertensive rats)

IT 50-99-7, Glucose, biological studies 9004-10-8, Insulin, biological RL: BSU (Biological study, unclassified); BIOL (Biological study) (GLP-1 effect on blood glucose and insulin in Dahl salt-sensitive hypertensive rats) IT 7440-23-5, Sodium, biological studies 7732-18-5, Water, biological RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GLP-1 effect on water and sodium excretion in Dahl
salt-sensitive hypertensive rats) Sarce-sensive mypertensive rats)
 Sarce-sensive mypertensive rats)
 Sarce-sensive mypertensive rats)
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive rats)
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Anderson, S; J Clin Invest 1985, V76, P612 CAPLUS (2) Barragan, J; Am J Physiol 1994, V266, PE459 CAPLUS (3) Bishop, J; Cardiovasc Res 2000, V47, P57 CAPLUS (4) Bullock, B; Endocrinology 1996, V137, P2968 CAPLUS (5) Campese, V; Hypertension 1994, V23, P531 MEDLINE

(6) Dall'Aglio, E, Am J Hypertens 1991, V4, P773 CAPLUS

Dahl salt-sensitive rats Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly, AUTHOR(S): Annette; Ditter, Katie; Mistry, Mahesh; Roman, Richard CORPORATE SOURCE: SOURCE: Department of Physiology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA SOURCE: Journal of Hypertension (2003), 21(6), 1125-1135 CODEN: JOHYD3; ISSN: 0263-6352 Lippincott Williams & Wilkins Journal PUBLISHER: DOCUMENT TYPE: LANGUAGE: English
AN 2003:447519 CAPLUS <<LOGINID::20070124>> DN 139:255595 Entered STN: 11 Jun 2003 TI Antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive AU Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly, Annette; Ditter, Katie; Mistry, Mahesh; Roman, Richard J.
CS Department of Physiology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA SO Journal of Hypertension (2003), 21(6), 1125-1135 CODEN: JOHYD3; ISSN: 0263-6352 PB Lippincott Williams & Wilkins DT Journal LA English
CC 2-6 (Mammalian Hormones) AB Dahl salt-sensitive (Dahl S) rats exhibit many phenotypic traits associated with salt-sensitive hypertension in man. Specifically, they are win satt-sensitive nypertension in man. Specifically, they are salt-sensitive, insulin-resistant and hypertipidemic. They also develop endothelial dysfunction, cardiac injury and glomerulosclerosis. Insulin resistance is linked to hypertension, renal and cardiac damage and endothelial dysfunction. Thus, an agent that has diuretic action and can improve insulin resistance, like recombinant glucagon-like peptide-1(7-36)amide (rGLP-1), may have an antihypertensive effect. To determine whether chronic administration of rGLP-1 attenuates the development of hypertension, endothelial dysfunction and/or hypertension-induced renal and cardiac end organ damage in Dahl S rats. Mean arterial pressure (MAP) and urinary excretion of protein and albumin were measured in Dahl S rats before and after they were fed a 8% NaCl diet and infused with rGLP-1 (1 before and after they were ted a 8% NaCl diet and infused with RCLP-1 mg/kg per min, i.v.) or whicle for 14 days. At the end of the study, the degree of renal and cardiac injury was histol. assessed and endothelium-dependent relaxing function was studied using sortic rings. In other rats, the effects of rClP-1 on sodium and water balance and plasma glucose and insulin levels for the first 3 days following a step change in sodium intake from a 0.1% NaCl diet to 7.5 mEq/day were determined

The rGLP-1 significantly attenuated the development of hypertension in Dahl S rats (136 vs. 174 mmHg). This was associated with reduction in proteinuria (46 vs. 128 mg/day) and albuminuria (46 vs. 86 mg/day) and improvement of endothelial function and renal and cardiac damage. The rGLP-1 markedly increased urine flow and sodium excretion for the first 3 Adays following elevation in sodium intake. It had no significant effects on plasma glucose and insulin concus. The rGLP-1 has antihypertensive and cardiac and renoprotective effects in Dahl S rats fed a high salt diet. The antihypertensive effect of rGLP-1 in Dahl S rats is due mainly to its diuretic and natriuretic effects, rather than an effect to improve

insulin-resistance.

ST hypertension GLP1; sodium water excretion hypertension GLP1; glucose insulin blood hypertension GLP1; acuta heart kidney damage hypertension GLP1; albuminuria proteinuria hypertension GLP1; antihypertensive GLP1 diuresis natriuresis

IT Hypertension

(Dahl salt-sensitive; antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive rats)

IT Heart, disease Kidney, disease

(GLP-1 effect on aorta endothelium and heart and kidney damage in Dahl salt-sensitive hypertensive rats)

IT Blood pressure

Heart rate
(GLP-1 effect on blood pressure and heart rate in

Oah salt-sensitive hypertensive rats)

Albumins, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(albuminuria; GLP-1 effect on albuminuria and
proteinuria in Dahl salt-sensitive hypertensive rats)

IT Antihypertensives

(antihypertensive action of GLP-1 in Dahl

salt-sensitive hypertensive rats is due to diuretic and natriuretic

actions)

IT Artery, disease
(aortic endothelial injury; GLP-1 effect on aorta

endothelium and heart and kidney damage in Dahl salt-sensitive hypertensive rats)

(aortic endothelial; GLP-1 effect on aorta

endothelium and heart and kidney damage in Dahl salt-sensitive

hypertensive rats)

Endothelium

(aortic, disease, injury; GLP-1 effect on aorta endothelium and heart and kidney damage in Dahl salt-sensitive

hypertensive rats)

(25) Nauck, M; Exp Clin Endocrinol Diabetes 1997, V105, P187 CAPLUS (26) Orskov, C; Diabetes 1994, V43, P535 CAPLUS (27) O'Bryan, G; Semin Nephrol 1997, V17, P93 CAPLUS (28) Parving, H; Lancet 1983, V1, P1175 MEDLINE (29) Raij, L; Am J Med 1985, V79, P37 CAPLUS (30) Rapp, J; Hypertension 1982, V4, P753 MEDLINE (31) Reaven, G; Hypertension 1991, V18, P630 CAPLUS (32) Ritz, E; J Intern Med 1999, V245, P111 MEDLINE (33) Roman, R; Am J Hypertens 1997, V10, P63S CAPLUS (34) Sakamoto, S; Diabetes 1998, V47, P82 CAPLUS (35) Salonen, J; Diabetes 1998, V47, P82 CAPLUS (35) Salonen, J; Diabetes 1998, V47, P270 CAPLUS (36) Shimabukuro, M; Metabolism 1996, V45, P1168 CAPLUS (37) Sterzel, R; Kidney Int 1988, V33, P1119 MEDLINE (38) Tierney, W; Am J Kidney Dis 1989, V13, P485 MEDLINE (39) Tobian, L; Hypertension 1979, V1, P316 CAPLUS (40) Toft-Nielsen, M; Diabetes Care 1999, V22, P1137 MEDLINE (41) Vella, A; Diabetes 2000, V49, P611 CAPLUS

(41) Vella, A; Diabetes 2000, V49, P611 CAPLUS (42) Yagi, K; Hypertension 1997, V29, P728 CAPLUS (43) Yamamoto, H; J Clin Invest 2002, V110, P43 CAPLUS (44) Zou, A; Hypertension 1996, V27, P631 CAPLUS

=> D Ibib 130

L30 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: DOCUMENT NUMBER: 2003:447519 CAPLUS <<LOGINID::20070124>> 139:255595

Antihypertensive effect of glucagon-like peptide 1 in Dahl salt-sensitive rats

AUTHOR(S):

Yu, Ming; Moreno, Carol; Hoagland, Kimberly M.; Dahly, Annette; Ditter, Katie; Mistry, Mahesh; Roman, Richard

SOURCE: Department of Physiology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA CORPORATE SOURCE:

Journal of Hypertension (2003), 21(6), 1125-1135

SOURCE:

CODEN: JOHYD3; ISSN: 0263-6352 Lippincott Williams & Wilkins

PUBLISHER: DOCUMENT TYPE: Journal

LANGUAGE: English
REFERENCE COUNT: 44
AVAILABLE TO THE PROPERTY OF THE PROPERT 44 THERE ARE 44 CITED REFERENCES

AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D Ibib Ali L33 1-9

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (proteinuria; GLP-1 effect on albuminuria

and proteinuria in Dahl salt-sensitive hypertensive rats)

IT 50-99-7, Glucose, biological studies 9004-10-8, Insulin, biological

RL: BSU (Biological study, unclassified); BIOL (Biological study) (GLP-1 effect on blood glucose and insulin in Dahl salt-sensitive hypertensive rats)

IT 7440-23-5, Sodium, biological studies 7732-18-5, Water, biological

studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (GLP-1 effect on water and sodium excretion in Dahl salt-sensitive hypertensive rats)

IT 89750-14-1, Glucagon-like peptide 1 118549-37-4, Insulinotropin RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antihypertensive effect of glucagon-like peptide 1 in Dahl

salt-sensitive rats)

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD

(1) Anderson, S; J Clin Invest 1985, V76, P612 CAPLUS

RE
(1) Anderson, S; J Clin Invest 1985, V76, P612 CAPLUS
(2) Barragan, J; Am J Physiol 1994, V266, PE459 CAPLUS
(3) Bishop, J; Cardiovasc Res 2000, V47, P57 CAPLUS
(4) Bullock, B; Endocrinology 1996, V137, P2968 CAPLUS
(5) Campese, V; Hypertension 1994, V23, P531 MEDLINE
(6) Dall'Aglio, E; Am J Hypertens 1991, V4, P773 CAPLUS
(7) DeFronzo, R; Diabetologia 1981, V21, P165 CAPLUS
(8) DeFronzo, R; JClin Invest 1976, V58, P83 CAPLUS
(9) Dengel, D; Hypertension 1996, V28, P127 MEDLINE
(10) Epstein, M; Hypertension 1992, V19, P403 MEDLINE
(11) Ferrannini, E; N Engl J Med 1987, V317, P350 MEDLINE
(12) Greene, A; Am J Physiol 1990, V258, PH508 MEDLINE
(13) Grim, C; Hypertension 1990, V15, P803 MEDLINE
(14) Hayakawa, H; Circulation 1997, V96, P2407 CAPLUS
(15) Ito, O; Hypertension 1999, V31, P803 MEDLINE
(16) Katakam, P; Am J Physiol 1998, V275, PR788 CAPLUS
(17) Kim, S; Br J Pharm 1996, V118, P549 CAPLUS
(18) Kotchen, T; Am J Hypertens 1997, V10, P1020 CAPLUS
(19) Kotchen, T; Am J Physiol 1991, V261, PE692 CAPLUS
(20) Miller, A; J Cardiovasc Pharm Ther 1998, V3, P125 CAPLUS
(21) Minireview, D; Endocrinology 2001, V142, P521
(22) Mogensen, C; Scand J Clin Lab Invest 1976, V36, P383 MEDLINE
(23) Mondon, C; Metabolism 1988, V37, P303 CAPLUS

L33 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2004:533962 CAPLUS <<LOGINID::20070124>>

DOCUMENT NUMBER: 141:82335

Human glucagon-like-peptide-1 mimics and their

antidiahetic effects

INVENTOR(S):): Natarajan, Sesha Iyer, Mapelli, Claudio; Bastos, Margarita M.; Bernatowicz, Michael; Lee, Ving; Ewing,

William R. Dernatuwicz, Michael, Lee, Ving, Ewing, William R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S.
Ser. No. 273,975.

CODEN: USXXCO

DOCUMENT TYPE: LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE US 2003-419399

US 2003195157 A1 20031016 US 2002-273975 20021018 <--A2 20041104 A3 20050915 WO 2004-US12374

WO 2004094461

// O 2004094461 A3 20050915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, LS, YY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, ZZ, MD, PIL TL TM, AT BR BG, CH, CY, CZ, DB, DE, FE

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CL, CM, GA, GN, GQ, GW, ML, MR, NE, SN,

EP 1615653 A2 20060118 EP 2004-760098 20040421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LL, LU, NL, SE, MC, PT,
EE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
PRIORITY APPLN. INFO.: US 2001-342015P P 20011018
US 2002-273975 A2 20021018
US 2003-419399 A 20030421
WO 2004-US12374 W 20040421
AN 2004:533962 CAPLUS <<LOGINID::20070124>>
DN 141:82335 FP 1615653 A2 20060118 EP 2004-760098

ED Entered STN: 02 Jul 2004

TI Human glucagon-like-peptide-I mimics and their antidiabetic effects IN Natarajan, Sesha lyer, Mapelli, Claudio; Bastos, Margarita M.;

```
PA USA
SO U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 273,975.
           CODEN: USXXCO
 DT Patent
  LA English
IC ICM A61K038-10
ICS C07K007-08
  INCL 514015000; 530328000
 CC 1-10 (Pharmacology)
Section cross-reference(s): 2, 34, 63
FAN.CNT 2
            PATENT NO.
                                                                                        KIND DATE
                                                                                                                                                               APPLICATION NO.
                                                                                        A1 20040701 US 2003-419399
A1 20031016 US 2002-273975
A2 20041104 WO 2004-US12374
A3 20050915
 PI US 2004127423
                                                                                                                                                                                                                                                   20030421
             US 2003 195 157
                                                                                                                                                                                                                                               20021018
             WO 2004094461
                                                                                                                                                                                                                                                          20040421
                    /O 2004094461 A3 20050915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, FG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, FT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                                                                   A2 20060118 EP 2004-760098
            EP 1615653
                      E. AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
         E. 31, LVVIII, WARDEN BY STANDARD BY STAND
 PRAI US 2001-342015P
 CLASS
   PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES
  US 2004127423 ICM A61K038-10
ICS C07K007-08
INCL 514015000; 530328000
                                         IPCI A61K0038-10 [ICM,7]; C07K0007-08 [ICS,7]; C07K0007-00
                                        [ICS,7,C*]
IPCR A61K0038-00 [N,C*]; A61K0038-00 [N,A]; C07K0014-435
                                                     [I,C*]; C07K0014-605 [I,A]
```

Bernatowicz, Michael; Lee, Ving; Ewing, William R.

```
(MTP (microsomal triglyceride-exchanging protein), inhibitors; human glucagon-like-peptide-1 mimics and their antidiabetic effects)
    Antiarteriosclerotics
      (antiatherosclerotics; human glucagon-like-peptide-1 mimics and their
        ntidiahetic effects)
     Drug delivery systems
      (capsules; human glucagon-like-peptide-1 mimics and their antidiabetic
   RL: BSU (Biological study, unclassified); BIOL (Biological study) (cholesterol ester-exchanging; human glucagon-like-peptide-1 mimics and
      their antidiabetic effects)
     Kidney, disease
     (diabetic nephropathy; human glucagon-like-peptide-1 mimics and their antidiabetic effects)
IT Nerve, disease
      (diabetic neuropathy; human glucagon-like-peptide-1 mimics and their
       antidiabetic effects)
IT Eye, disease
      (diabetic retinopathy; human glucagon-like-peptide-1 mimics and their
      antidiabetic effects)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dopamine transporter, human glucagon-like-peptide-1 mimics and their
      antidiabetic effects)
IT 5-HT reuptake inhibitors
   Antihypertensives
Antiobesity agents
    Appetite depressants
    Atherosclerosis
    Diabetes mellitus
    Hyperglycemia
   Hypertension
    Hypertriglyceridemia
   Hypolipemic agents
Obesity
Signal transduction, biological
    Wound healing
   b3-Adrenoceptor agonists
(human glucagon-like-peptide-1 mimics and their antidiabetic effects)
IT Fatty acids, biological studies
   Glucagon-like peptide-1 receptors
   Hypertipidemia
Thyroid hormone receptors
```

RL: BSU (Biological study, unclassified); BIOL (Biological study)

```
[ICS,7]; COTK0007-06 [ICS,7]; COTK0007-00 [ICS,7,C*]

IPCR A61K0038-00 [N,C*]; A61K0038-00 [N,A]; C07K0014-435

[LC*]; C07K0014-05 [I,A]

NCL 514/016.000; 514/017.000; 530/328.000; 530/329.000
 NCL 514/016.000, 514/017.000; 530/328.000; 530/329.000
ECLA C07K014/605

WO 2004094461 IPCI C07K [ICM,7]

IPCR A61K0038-02 [L,C*]; A61K0038-06 [L,A]; A61K0038-02

[L,C*]; A61K0038-02 [L,A]; A61K0038-06 [L,C*]; A61K0038-10

[L,A]; C07K [L,S]; C07K0007-00 [L,C*]; A61K0038-10

[L,A]; C07K [L,S]; C07K0007-00 [L,C*]; C07K0007-02

[L,A]; C07K007-04 [L,A]; C07K0007-02 [L,S]; A61K0038-10

[ICS,7]; A61K0038-08 [ICS,7]; C07K0007-02 [ICS,7]; A61K0038-10

[ICS,7,C*]
CO7K0007-04 [ICS,7]; CO7K0007-08 [ICS,7]; CO7K0007-00 [ICS,7,0]]

IPCR A61K0038-00 [LC*]; A61K0038-00 [LA]; A61K0038-02 [LA]; A61K0038-02 [LA]; A61K0038-03 [LC*];

A61K0038-02 [LA]; A61K0038-10 [LC*]; A61K0038-10 [LA]; CO7K007-04 [LA]; CO7K0007-02 [LA]; CO7K0007-04 [LA]; CO7K0007-08 [LA]

AB The invention discloses human glucagon-like peptide-1 (GIP-1) peptide mirnies that mirnic the biol. activity of the native
      GLP-1 peptide and thus are useful for the treatment or
prevention of diseases or disorders associated with GLP activity. Further,
      the invention of useases of usonoters associated with GLF activity. Full the invention provides novel, chemical modified peptides that not only stimulate insulin secretion in type II diabetics, but also produce other beneficial insulinotropic responses. These synthetic peptide GLP—I mimics exhibit increased stability to proteolytic cleavage making them ideal therapeutic candidates for oral or parenteral
        administration
 ST human glucagon peptide mimic prepn diabetes antidiabetic insulin stability
       RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
(ALBP (adipocyte lipid-binding protein); human glucagon-like-peptide-1
           mimics and their antidiabetic effects)
           ipoprotein receptors
      RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LDL; human glucagon-like-peptide-1 mimics and their antidiabetic
          effects)
 IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
(human glucagon-like-peptide-1 mimics and their antidiabetic effects)
IT Peptides, biological studies
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
      (Uses)
          (human glucagon-like-peptide-1 mimics and their antidiabetic effects)
 IT Sulfonylureas
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
(human glucagon-like-peptide-1 mimics and their antidiabetic effects)
       Drug delivery systems
          (injections; human glucagon-like-peptide-1 mimics and their antidiabetic effects)
 IT Metabolic disorders
          (metabolic syndrome X; human glucagon-like-peptide-1 mimics and their
          antidiabetic effects)
        Drug delivery systems
         (microparticles; human glucagon-like-peptide-1 mimics and their antidiabetic effects)
IT Diabetes mellitus
          (non-insulin-dependent; human glucagon-like-peptide-1 mimics and their antidiabetic effects)
 IT Antidiabetic agents
      Drug delivery systems
          (oral; human glucagon-like-peptide-1 mimics and their antidiabetic
           effects)
IT Drug delivery systems
          (suspensions; human glucagon-like-peptide-1 mimics and their
          antidiabetic effects)
       Drug delivery syste
                blets; human glucagon-like-peptide-1 mimics and their antidiabetic
          effects)
     Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(a; human glucagon-like-peptide-1 mimics and their antidiabetic
          effects)
TT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(g; human glucagon-like-peptide-1 mimics and their antidiabetic
tridies 9001-62-1, Lipase 9028-35-7, 3-Hydroxy-3-methylglutaryl CoA reductase 9029-60-1, Lipoxygenase 9033-06-1, Glucosidase 9077-14-9, Squalene synthetase 63551-74-6, Lipoxygenase 90002-36-1, 2-Ethylphenyl
```

RL: BSU (Biological study, unclassified); BIOL (Biological study)

NCL 514/015.000: 530/328.000

ECLA C07K014/605 US 2003195157 IPCI A61K0038-10 [ICM,7]; A61K0038-08 [ICS,7]; C07K0007-08

```
(human glucagon-like-peptide-1 mimics and their antidiabetic effects)

IT $16514-32-2P $16514-38-8P $16514-43-5P $16514-47-9P $16514-62-6P $16514-52-6P $16514-75-3P $16514-75-9P $16514-47-9P $16514-48-4P $16514-7P $16514-79-19 $16514-93-PP $16514-64-0P $16514-68-4P $16515-47-7P $16514-19-3P $16514-95-PP $16514-81-1P $16515-30-0P $16515-60-3P $16515-90-6P $16515-34-7P $16515-30-3P $16515-34-7P $16515-30-3P $16515-34-7P $16515-32-3P $16515-68-1P $16515-50-7P $16515-50-7P $16515-50-7P $16515-50-PP $16515-50-PP $16515-68-1P $16515-68-1P $16515-72-3P $16515-59-6P $16515-68-7P $16515-52-7P $16515-59-6P $16515-68-3P $16515-68-1P $16516-614-6P $16516-18-0P $16516-61-0-P $16516-614-6P $16516-64-6P $16516-62-P $16516-64-6P $16516-63-6P $16516-50-0P $16516-55-9P $16516-35-1P $16516-64-6P $16516-64-P $16516-64-P $16516-64-P $16516-63-0P $16516-76-0P $16516-76-0P $16516-76-0P $16516-76-0P $16517-02-PP $16517-33-PP $16518-33-PP $16518-34-PP $16518-34-PP $16518-34-PP $16518-34-PP $16518-33-PP $16518-34-PP $16518-34-PP
```

```
RL: SPN (Synthetic preparation); PREP (Preparation)
(human glucagon-like-peptide-1 mimics and their antidiabetic effects) IT 9027-63-8, ACAT
   RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; human glucagon-like-peptide-1 mimics and their
       antidiabetic effects)
IT 54249-88-6, Dipeptidyl peptidase IV
   RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (inhibitors; human glucagon-like-peptide-1 mimics and their
antidiabetic effects)

IT 9004-10-8, Insulin, biological studies
   RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance, hyperinsulinemia; human glucagon-like-peptide-1 mimics and
      their antidiabetic effects)
L33 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:157498 CAPLUS <<LOGINID::20070124>>
DOCUMENT NUMBER: 140:199313
TITLE: Preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors

INVENTOR(S): Daisy, Do
PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Eur. Pat. Appl., 71 pp.
                   CODEN: EPXXDW
TYPE: Patent
DOCUMENT TYPE:
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:
                              English
   PATENT NO.
                             KIND DATE
                                                      APPLICATION NO.
                                                                                          DATE
   EP 1391460
                            A1 20040225 EP 2003-20676
                                                                                 20000918
       R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
          IE, FI, CY
   EP 1088824
                            A2 20010404 EP 2000-308131
                                                                                 20000918 <--
                            A3 20010627
   EP 1088824
                            B1 20040107
       R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
```

A1 20021205 US 2002-117370 B2 20030610

A1 20031016 US 2003-367002 B2 20041207

EP 2000-308131 A3 20000918

US 1999-157148P

20030214 <--

P 19990930

IE, SI, LT, LV, FI, RO

US 2002183369

US 2003195361

US 6576653

US 6828343 B2 2 PRIORITY APPLN. INFO.:

```
preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
         (Preparation); USES (USES)
(human glucagon-like-peptide-I mimics and their antidiabetic effects)
713497-9-1P 713497-81-5P 713497-83-7P 713497-85-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP
preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (human glucagon-like-peptide-1 mimics and their antidiabetic effects) IT 51-64-9, Dexamphet-amine 56-03-1, Biguanide 94-20-2, Chloropropamide 122-09-8, Phentermine 637-07-0, Clofbrate 657-24-9, Metformin 943-45-3D, Fibric acid, derivs. 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 21187-98-4, Gliclazide 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-611-9, Glipizide 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 56180-94-0, Acarbose 72432-03-2, Miglitol 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 89750-14-1, Glucagon-like peptide 1 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 9829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 105816-04-4, Nateglinide 106650-56-0,
       93957-54-1, Fluvastatin 96829-58-2, Crlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 134523-00-5, Ator-vastatin 135062-02-1, Repaglinide 141750-63-2, Nisvastatin 141758-74-9, AC2993 142288-97-1, TS-962 145599-86-6, Cerivastatin 152755-31-2, LY295427 159183-92-3, L750355 161600-01-7, lagglitazone 165818-60-1, Avasimbe 1708161-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 198608-45-4 199113-98-9, NN-2344 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 258345-41-4, GW-409544 262352-17-0, CP 529414 282526-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-17-2, AR-H039242 335149-23-0, NVP-DPP-728A
 KAD1129 315149-17-2, AR-HO39242 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipyride 444069-80-1, Axokine RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (human glucagon-like-peptide-1 mimics and their antidiabetic effects) T 150-46-9, Triethylborate 358-23-6, Triflic anhydride 1973-22-4, 1-Bromo-2-ethylbenzene 4326-36-7 16419-60-6, O-Tolylboronic acid 82911-69-1 93267-04-0 516521-49-6 713497-86-0
  RL: RCT (Reactant); RACT (Reactant or reagent)
(human glucagon-like-peptide-1 mimics and their antidiabetic effects)

IT 112766-18-4P 516521-46-3P 516521-47-4P 516521-48-5P 516521-50-9P
         RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
  (Reactan or reagent)
(human glucagon-like-peptide-1 mimics and their antidiabetic effects)

Tr 713497-87-1P 713497-88-2P
                                                                US 2000-670759 A3 20000927
                                                                US 2002-117370
                                                                                                               A3 20020405
                                                                   MARPAT 140:199313
   OTHER SOURCE(S):
  AN 2004:157498 CAPLUS <<LOGINID::20070124>>
DN 140:199313
   ED Entered STN: 26 Feb 2004
  TI Preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors
  IN Daisy, Joe
PA Pfizer Products Inc., USA
  SO Eur. Pat. Appl., 71 pp.
CODEN: EPXXDW
  DT Patent
  LA English
IC ICM C07D495-04
        ICS C07D491-04; C07D209-52; A61K031-407; A61P003-10; A61P009-10; C07D495-14; C07D333-00; C07D209-00; C07D307-00
   CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
   FAN.CNT 2
         PATENT NO.
                                                       KIND DATE APPLICATION NO.
             EP 1391460 A1 20040225 EP 2003-20676 20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
   PI EP 1391460
         IE, FL, CY
EP 1088824
                                                    A2 20010404 EP 2000-308131
                                                                                                                                                20000918 <--
         EP 1088824
EP 1088824
                                                    A3 20010627
B1 20040107
         E: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LL, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
US 2002183369 A1 20021205 US 2002-117370 20020405 <--
         US 6576653
US 2003 195361
B2 20030610
                                                                                                                                                     20030214 <--
   PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES
   EP 1391460
                                     ICM C07D495-04
                                   C07D491-04; C07D209-52; A61K031-407; A61P003-10; A61P009-10; C07D495-14; C07D333-00; C07D209-00;
                          ICS
                                    C07D307-00
```

IPCI C07D0495-04 [ICM,7]; C07D0491-04 [ICS,7]; C07D0491-00

516521-54-3P 516521-55-4P 713497-71-3P 713497-72-4P 713497-73-5P 713497-74-6P 713497-75-7P 713497-77-9P RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic

```
[ICS,7,C*]; C07D0209-52 [ICS,7]; A61K0031-407 [ICS,7];
A61P0003-10 [ICS,7]; A61P0003-00 [ICS,7,C*];
A61P0009-10 [ICS,7]; A61P0009-00 [ICS,7,C*];
C07D0495-14 [ICS,7]; C07D0495-00 [ICS,7,C*];
C07D0333-00 [ICS,7]; C07D0209-00 [ICS,7]; C07D0307-00
                                                                          [ICS,7]
ECLA C07D491/04+307B+209B; C07D495/04+333B+209B;
                                                                   [ICS,7]
ECLA CO7D491/04+307B+209B; C07D495/04+333B+209B;
C07D495/14+333B+33B+209B
824 IPC1 CO7D0495-04 [ICM,6]; C07D0491-04 [ICS,6]; C07D0209-52 [ICS,6]; A61F0003-10 [ICS,6]; A61F0003-10 [ICS,6]; A61F0009-10 [ICS,6]; A61F0009-00 [ICS,6,C*]; A61F0009-10 [ICS,6]; C07D0495-04 [ICL,6]; C07D0495-00 [ICL,6]; C07D0495-04 [ICL,6]; C07D0495-00 [ICL,6]; C07D0491-04 [ICL,6]; C07D0491-00 [ICL,6]; C07D0491-048 [IA]; A61K0031-407 [IA]; A61K0031-427 [IA]; A61K0031-427 [IA]; A61K0031-427 [IA]; A61K0031-4523 [IC*]; A61K0031-452 [IA]; A61K0031-452 [IA]; A61K0031-452 [IA]; A61K0031-452 [IA]; A61K0031-452 [IA]; A61K0031-455 [IA]; A61K0031-452 [IA]; A61K0031-455 [IA]; A61K0031-452 [IA]; A61K0031-455 [IA]; A61K0031-452 [IA]; A61K0031-455 [IA]; A61F0031-455 [IA]; A61F0031-45 [IA]; A61F0031-
[I,C*]; CO7F0007-10 [I,A]; CU/KUUD-UU [I,C*];

CO7K0005-00 [I,A]

ECLA CO7D209/52; CO7D491/04+307B+209B; CO7D495/04+333B+209B

US 2002183369 PCI CO7D0513-22 [ICM,7]; CO7D0513-00 [ICM,7,C*];

A61K0031-429 [ICS,7]; A61K0031-424 [ICS,7];

A61K0031-4188 [ICS,7]; A61K0031-4164 [ICS,7,C*]

IPCR CO7D0209-00 [I,C*]; CO7D0209-52 [I,A]; CO7D0491-00

[I,C*]; CO7D0491-04 [I,A]; CO7D0495-00 [I,C*];

CO7D0406-04 II A1
                                                                          C07D0495-04 [LA]
NCL 514/367.000; 514/375.000; 514/393.000; 514/412.000;
NCL 514/367.000; 514/375.000; 514/393.000; 514/412.000; 548/153.000; 548/217.000; 548/213.000; 548/217.000; 548/33.01.00; 548/453.000 ECLA C07D209/52; C07D491/04+307B+209B; C07D495/04+333B+209B US 2003195361 PCI C07D0513-12 [ICM,7]; C07D0498-02 [ICS,7,C*]; C07D0513-02 [ICS,7,C*]; C07D0487-02 [ICS,7]; C07D0487-00 [ICS,7,C*] PCR C07D0209-00 [I,C*]; C07D0497-02 [I,A]; C07D0491-00 [I,C*]; C07D0491-04 [I,A]; C07D0495-00 [I,C*];
                                                                                                       C07D0495-04 [LA]
```

```
(diabetic nephropathy, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
      Nerve, disease
(diabetic neuropathy, treatment; preparation of fused pyrrolylcarboxamides
        as glycogen phosphorylase inhibitors)
      Eye, disease
       (diabetic retinopathy, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
IT Antioxidants
       (fatty acid oxidation inhibitors coadministration; preparation of fused
        pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
IT Gluconeogenesis
       Citiconeogenesis
(inhibitors coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
       (ischemia, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
IT Anti-ischemic agents
     Anticholesteremic agents
     Antidiabetic agents
     Antihypertensives
Drug delivery systems
     Hypolipemic agents
        (preparation of fused pyrrolylcarboxamides as glycogen phosphorylase
IT Atherosclerosis
     Cataract
     Diabetes mellitus
     Hypercholesterolemia
     Hyperglycemia
      Typertriglyceridemia
     Ischemia
       (treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)
IT Hyperlipidemia
    RL: BSU (Biological study, unclassified); BIOL (Biological study) (treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

The Peroxisone proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(g. PPAR-g agonists coadministration; preparation of fused pyrrolylearboxamides as glycogen phosphorylase inhibitors)
```

hosphorylase inhibitors)

IT Kidney, disease

NCL 548/153.000; 548/218.000; 548/303.100; 548/453.000 ECLA C07D209/52; C07D491/04+307B+209B; C07D495/04+333B+209B OS MARPAT 140:199313

AB Title compds. [I; Q = substituted aryl, heteroaryl; Z, X = C, CH, CH2, N, O, S; X1 = NRa, CH2, O, S; dotted lines = bond, null; both dotted lines are not simultaneously bonds; R1 = H, halo, alkoxy, alkylthio, alkyl, CF3, NH2, alkylamino, dialkylamino, NO2, CN, CO2H, carboxyalkyl, alkenyl, alkynyl; Ra, Rb = H, alkyl; Y = CH(OH), null; R2R3 = atoms to form a 5-6 membered ring containing 0-3 heteroatoms and 0-2 double bonds; R4 = COA; A = NRdRd, NRaCH2CH2ORa, N-heterocycly; Rd = H, alkyl, alkoxy, aryl, (substituted) aryl, heteroaryl; Rc = H, CO2Ra, ORa, SRa, NRaRa; n = 1-3], were prepared for treatment of diabetes, insulin resistance, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, cataracts, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hypertipidemia, atherosclerosis, or tissue ischemia (no cataracts, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis, or tissue ischemia (no data). Thus, 6H-thieno(2,3-b]pyrrole-5-carboxylic acid and (3S)-amino-1-((3R,4S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-4-phenylbutan-1-one were coupled using 4-{dimethylaminoppyyl-3-ethylcarbodimide hydrochloride in CH2Cl2/DMF to give 6H-thieno[2,3-b]pyrrole-5-carboxylic acid [(1S)-benzyl-3-((3R,4S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-3-axpnoryllamide.

nephropathy retinopathy cataract hyperglycemia hypercholesterolemia hypertension treatment pyrrolecarboxamide; hyperinsulinemia hyperlipidemia atherosclerosis tissue ischemia treatment fused pyrrolecarboxamide

(cardiac, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

IT Antiobesity agents a2-Adrenoceptor antagonists

b-Adrenoceptor agonists
(coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

Sulfonylureas
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; preparation of fused pyrrolylcarboxamides as glycogen

```
IT 9007-92-5, Glucagon, biological studies 106602-62-4, Amylin
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists coadministration; preparation of fused pyrrolylcarboxamides as
glycogen phosphorylase inhibitors)
```

tanagomisis cuaministration; preparation of fused pyrrolytearboxamides as glycogen phosphorylase inhibitors.

T 56-03-1D, Biguanide, derivs. 64-77-7, Tolbutamide 94-20-2, Chloroproparunide 114-86-3, Phenformin 458-24-2, Fenfluramine 657-24-9, Metformin 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 2295-31-0D, Thiazolidinedione, derivs. 7440-62-2D, Vanadium, complexes 9004-10-8, Insulin, biological studies 9004-10-8D, Insulin, analogs 10238-21-8, Glibenclamide 12179-36-1D, Pervanadyl (VO(Q2)+), complexes 23602-78-0, Benfluorex 28299-33-4D, Imidazoline, derivs. 29094-61-9, Glipizide 3735-33-14, Vanadate 51037-30-0, Acipimox 51110-01-1D, Somatostatin, analogs 54870-28-9, Meglitini 4772-77-3, Ciglitaxone 73558-37-1, Linogliride 79944-58-4, Idazoxan 80879-63-6, Emiglitate 83480-29-9, Voglibose 86615-96-5, BRL35135 88431-47-4, Clomoxir 89197-32-0, Efaroxan 90505-66-1, Ro 16-8714 90730-96-4, BRL37344 93479-97-1, Glimepiride 97322-87-7, Troglitazone 104343-33-1, MDL-25637 105182-45-4, Fluparoxan 105816-04-4, Nateglinide 106612-94-6, Human GLP-1 (7-37) 107444-51-9, Rat GLP-1(7-36)amide 109229-58-5, Englitazone -(7-37) 107444-51-9, Rat GLP-I(7-36)amide 109229-58-5, Englitazone 110605-64-6, Isaglidole 111025-46-8, Pioglitazone 115656-32-1, D 7114 11000-04-6, Isagiidote 11102-46-8, Progritazone 11505-02-1, L 122330-73-4, Rosiglitazone 12257-28-4, Naglivan 122830-14-2, Deriglidole 124083-20-1, Etomoxir 127214-23-7, Camiglibose 130714-47-5, WAG 994 133107-64-9, Insulin lispro 135062-02-1, Repaglinide 138908-40-4, CL 316243 141200-24-0, Darglitazone 141758-74-9, AC2993 187887-46-3, Symlin 395214-16-1 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; preparation of fused pyπolylcarboxamides as glycogen phosphorylase inhibitors)

The second relation of the second relation of the second relations relations of the second relations relation

(inhibitors coadministration, preparation of tused pyrrolyicarboxat glycogen phosphorylase inhibitors)

IT 9035-74-9, Glycogen phosphorylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of fused pyrrolylcarboxamides as glycogen
phosphorylase inhibitors)

TT 332098-11-0P 332098-12-1P 332098-13-2P 332098-14-3P 332098-15-4P 332098-16-5P 332098-17-6P 332098-18-7P 332098-19-8P 332098-20-1P 332098-21-2P 332098-23-4P 332098-24-6P 332098-26-7P 332098-27-8P 332098-28-9P 332098-29-0P 332098-30-3P 332098-31-4P 332098-32-5P 332098-33-6P 332098-34-7P 332098-35-8P 332098-36-9P 332098-37-0P 332098-38-1P 332098-39-2P 332098-40-5P 332098-41-6P 332098-42-7P 332098-43-8P 332098-44-9P 332098-45-0P 332098-46-1P 332098-47-2P 332098-48-3P 332098-49-4P 332098-50-7P

```
332098-52-9P 332098-54-1P 332098-55-2P 332098-57-4P 332098-59-6P 332098-61-0P 332098-63-2P 332098-65-4P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

IT 637-81-0, Azidoacetic acid ethyl ester 1066-54-2, (Trimethylsily)]acetylene 1126-09-6, Piperidine-4-carboxylic acid ethyl ester 4530-18-1, Boc-DL-Phenylalanine 6030-36-0, 4-Methylthiophene-2-carboxaldehyde 7283-96-7, 5-Chlorothiophene-2-carboxaldehyde 13679-70-4, 5-Methyl-2-thiophenecarboxaldehyde 13734-34-4, Boc-L-Phenylalanine 14345-97-2, 2-Chloro-3-methylthiophene 17186-57-1 18791-75-8, 4-Bromothiophene-2-carboxaldehyde 21508-19-0, 5-Chlorofuran-2-carboxaldehyde 21921-76-6, 4-Bromo-2-furaldehyde 24445-35-0 29669-49-6, 5-Fluorothiophene-2-carboxaldehyde 31486-85-8, Thieno(2,3-b)thiophene-2-carboxaldehyde 31486-85-8, Thieno(2,3-b)thiophene-2-carboxaldehyde 37-5-63-3, 6H-Thieno[3,2-b)pyrrole-5-carboxylic acid ethyl ester 39793-31-2, 4H-Thieno[3,2-b)pyrrole-5-carboxylic acid 51856-25-8, 6H-Thieno(2,3-b)pyrrole-5-carboxylic acid ethyl ester 75700-51-3, 4-Chlorothiophene-2-carboxylic acid 51856-29-2, 2-Formyl-6H-thieno[2,3-b)pyrrole-5-carboxylic acid ethyl ester 75700-51-3, 4-Chlorothiophene-2-carboxylic acid ethyl ester 91545-55-0, 2-Bromo-6H-thieno[2,3-b)pyrrole-5-carboxylic acid 80709-83-7, 2-Bromo-4H-furo[3,2-b)pyrrole-5-carboxylic acid 80709-83-7, 2-Bromo-4H-furo[3,2-b)pyrrole-5-carboxylic acid 80709-83-7, 2-Bromo-4H-thieno[3,3-b)pyrrole-5-carboxylic acid ethyl ester 105181-72-4, (2R,35)-3-tert-Butoxycarbonylamino-2-hydroxy-4-phenylbutyric acid 80709-83-7, 2-Bromo-4H-thieno[3,2-b)pyrrole-5-carboxylic acid ethyl ester 105181-72-4, (2R,35)-3-tert-Butoxycarbonylamino-2-hydroxy-4-phenylbutyric acid 80709-83-7, 2-Bromo-4H-thieno[3,2-b)pyrrole-5-carboxylic acid ethyl ester 105181-72-4, (2R,35)-3-tert-Butoxycarbonylamino-2-hydroxy-4-phenylbutyric acid 80709-83-80-80-80-80-80-80-80-80-80-8
```

DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

```
PATENT NO.
                                                                                       KIND DATE
                                                                                                                                                            APPLICATION NO.
                                                                                           A2 20030724
                                                                                                                                                            WO 2002-DK888
                                                                                                                                                                                                                                                 20021220 <--
WO 2003059372 A2 20030724 WO 2002-DK888 20021220 <--
WO 2003059372 A3 20040325

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, S, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SL, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2002351753 A1 20030730 AU 2002-351753 20021220 <--
EP 1461070 A2 20040929 EP 2002-787467 20021220 <--
EP 1461070 A2 20040929 PP 2002-787467 20021220 <--
EP 1461070 A2 20040929 PP 2003-559533 20021220

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

JP 2005516968 T 20050609 JP 2003-559533 20021220

US 2003144206 A1 20030731 US 2002-328282 20021223 <--
PRIORITY APPLN. INFO: DK 2001-1969 A 20011229

US 2002-350087P P 20020117

WO 2002-DK 888 W 20021220

AN 2003:570833 CAPLUS <<-->
LOGINID::20070124>>
DN 139:111682

ED Entered STN- 25 Inl 2003
                WO 2003059372
                                                                                            A3 20040325
   DN 139:111682
ED Entered STN: 25 Jul 2003
   TI Combined use of a GLP-1 compound and a modulator of diabetic late complications
  IN Knudsen, Lotte Bjerre; Selmer, Johan PA Novo Nordisk A/S, Den. SO PCT Int. Appl., 22 pp. CODEN: PIXXD2
    DT Patent
   LA English
IC ICM A61K038-00
   CC 1-10 (Pharmacology)
Section cross-reference(s): 2, 63
   FAN.CNT I
              PATENT NO.
                                                                                     KIND DATE
                                                                                                                                                           APPLICATION NO.
```

```
acid 332099-09-9P, 2-Bromo-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-11-3P, 2-Bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid 332099-16-8P, 2-Cyano-6H-thieno[2,3-b]pyrrole-5-carboxylic acid 332099-16-8P, 2-Cyano-6H-thieno[2,3-b]pyrrole-5-carboxylic acid 332099-18-0P 332099-20-4P 332099-24-8P, 2-Fluoro-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-28-2P, 2-Fluoro-4H-furo[3,2-b]pyrrole-5-carboxylic acid 332099-28-2P, 2-Chloro-4H-furo[3,2-b]pyrrole-5-carboxylic acid 332099-28-2P, 2-Chloro-4H-furo[3,2-b]pyrrole-5-carboxylic acid 4thyl ester 332099-39-3P, 3-Chloro-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-31-7P, 3-Chloro-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 4thyl ester 332099-31-7P, 3-Chloro-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 4thyl ester 332099-36-2P, 3-Bromo-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 4thyl ester 332099-36-2P, 3-Bromo-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 4thyl ester 332099-34-4-2P, 3-Methyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-42-0P, 3-Methyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-46-4P, 2-Formyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-46-4P, 2-Formyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-46-4P, 2-Formyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-52-2P, 3-Bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid 332099-60-2P 332099-52-2P, 3-Bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid 332099-60-2P 332099-52-2P, 3-Bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid 332099-60-2P 332099-60-2P 332099-60-2P 332099-60-2P 332099-60-2P 332099-60-2P 332099-60-2
```

```
PI WO 2003059372 A2 20030724 WO 2002-DK888 20021220 <--
WO 2003059372 A3 20040325

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2002351753 A1 20030730 AU 2002-351753 20021220 <--
EP 1461070 A2 20040929 EP 2002-787467 20021220

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

JP 2005516968 T 20050609 JP 2003-559533 20021220

US 2003144206 A1 20030731 US 2002-328282 20021223 <--

PRAI DK 2001-1969 A 20011229

DK 2002-760 A 20020517

WO 2002-DK888 W 20021220

CLASS

PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

WO 2003059372 ICM A61K038-00

IPCI A61K0031-05 [LC*]; A61K0031-167 [LC*]; A61K0031-138 [LC*]; A61K0031-165 [LC*]; A61K0031-167 [LC*]; A61K0031-35 [LC*]; A61K0031-401 [LC*]; A61K0031-401 [LC*]; A61K0031-401 [LC*]; A61K0031-401 [LC*]; A61K0031-407 [LA]; A61K0031-4166 [LA]; A61K0031-4164 [LC*]; A61K0031-4196 [LC*]; A61K0031-4164 [LC*]; A61K0031-4188 [LA]; A61K0031-4196 [LC*]; A61K0031-4196 [LA]; A61K0031-4196 [LA]; A61K0031-4196 [LA]; A61K0031-4196 [LA]; A61K0031-4196 [LA]; A61K0031-4196 [LA]; A61K0031-4196 [LC*]; A61K0031-4196 [LA]; A61K0031-4196 [LA]; A61K0031-4196 [LC*]; A61K0031-4196 [LA]; A61K0031-4196 [LA]; A61K0031-4196 [LA]; A61K0031-4196 [LA]; A61K0031-4196 [LA]; A61K0031-4196 [LA]; A61K0031-4196 [LC*]; A61K0031-4196 [LA]; A61K
```

```
[I.C*]; A61P0025-00 [I.A]; A61P0025-02 [I.A];
A61P0027-00 [I.C*]; A61P0027-02 [I.A]; A61P0043-00
[I.C*]; A61P0043-00 [I.C*];
AU 2002351753 [PCI A61K0035-00 [ICM,7]
[PCR A61K0035-00 [I.C*]; A61K0035-00 [I.A]; A61K0031-138
[I.C*]; A61K0031-165 [I.A]; A61K0031-165 [I.C*];
A61K0031-165 [I.A]; A61K0031-167 [I.C*]; A61K0031-167
[I.A]; A61K0031-32 [I.C*]; A61K0031-167 [I.C*]; A61K0031-167
[I.C*]; A61K0031-401 [I.A]; A61K0031-403 [I.C*];
A61K0031-403 [I.A]; A61K0031-403 [I.C*];
A61K0031-403 [I.A]; A61K0031-404 [I.A]; A61K0031-407
[I.C*]; A61K0031-407 [I.A]; A61K0031-404 [I.A]; A61K0031-4188
[I.A]; A61K0031-4166 [I.A]; A61K0031-4172 [I.A]; A61K0031-4188
[I.A]; A61K0031-4166 [I.A]; A61K0031-4172 [I.A]; A61K0031-4188
[I.A]; A61K0031-4196 [I.C*]; A61K0031-4172 [I.A]; A61K0031-5375
[I.C*]; A61K0031-537 [I.A]; A61K0031-472 [I.A]; A61K0031-5375
[I.C*]; A61K0031-577 [I.A]; A61K0031-57 [I.C*];
A61K0031-612 [I.C*]; A61K0033-26 [I.A];
A61P003-00 [I.C*]; A61P003-10 [I.A]; A61P0009-00
[I.C*]; A61P003-00 [I.A]; A61P0003-10 [I.A]; A61P0003-00
[I.C*]; A61P003-00 [I.A]; A61P0003-10 [I.A]; A61P003-00
[I.C*]; A61P003-00 [I.A]; A61P003-20 [I.A]; A61P003-00
[I.C*]; A61P003-00 [I.A]; A61K0031-35 [I.C*]; A61P003-10
[I.C*]; A61K0031-31 [I.A]; A61K0031-165 [I.C*]; A61K0031-165 [I.C*]; A61K0031-165 [I.A]; A61K0031-167 [I.A]; A61K0031-165 [I.A]; A61K0031-167 [I.A]; A61K0031-167 [I.A]; A61K0031-169 [I.A]; A61K0031-109 [I.C*]; A61K0031-109 [I.A]; A61K0031-109 [I.C*]; A61K0031-109 [I.A]; A61K0031-109 [I.A]; A61K0031-109 [I.A
```

```
4C086/NA05; 4C086/NA06; 4C086/ZA02; 4C086/ZA26; 4C086/ZA33; 4C086/ZA36; 4C086/ZA42; 4C086/ZA81;
4C086/ZA33; 4C086/ZA36; 4C086/ZA42; 4C086/ZA81;
4C086/ZC0; 4C086/ZC35; 4C086/ZC42; 4C206/AA01;
4C206/AA02; 4C206/RA18; 4C206/RA19; 4C206/RA21;
4C206/GA01; 4C206/GA31; 4C206/KA01; 4C206/MA02;
4C206/MA04; 4C206/MA11; 4C206/MA72; 4C206/MA75;
4C206/MA05; 4C206/MA06; 4C206/ZA02; 4C206/ZA26;
4C206/ZA33; 4C206/ZA36; 4C206/ZA42; 4C206/ZA81;
4C206/ZA06/ZC0; 4C206/ZC35; 4C206/ZC42; 4C206/ZA81;
4C206/ZA06/ZC0; 4C206/ZC35; 4C206/ZA42; 4C206/ZA81;
4C206/ZA06/ZC0; 4C206/ZC35; 4C206/ZA42; 4C206/ZA81;
4C206/ZA00; 4C206/ZA36; 4C206/ZA42; 4C206/ZA81;
4C206/ZA00; 4C206/ZA36; 4C206/ZA42; 4C206/ZA81;
4C206/ZA03; 4C206/ZA35; 4C206/ZA42; 4C206/ZA81;
4C206/ZA03; 4C206/ZA35; 4C206/ZA42; 4C206/ZA81;
4C206/ZA03; 4C206/ZA35; 4C206/ZA42; 4C206/ZA81;
4C206/ZA02; 4C206/ZA35; 4C206/ZA42; 4C206/ZA81;
4C206/ZA02; 4C206/ZA02; 4C206/ZA22; 4C206/ZA81;
4C206/ZA02; 4C206/ZA02; 4C206/ZA22; 4C206/ZA22;
4C206/ZA02; 4C206/ZA02; 4C206/ZA02; 4C206/ZA22;
4C206/ZA02; 4C206/Z
                  diabetic complications.
    ST GLP1 diabetes late complication therapy; glucagon like peptide I analog
                  fragment antidiabetic
    IT Angiotensin receptor antagonists
                  Antihypertensives
                  Humar
                    Hypertension
                    Protein sequences
                    b-Adrenoceptor antagonists
                 b1-Adrenoceptor antagonists
(combined use of a GLP-1 compound and a modulator of
                              diabetic late complications)
                      Kidney, disease
                          (diabetic nephropathy; combined use of a GLP-
                              I compound and a modulator of diabetic late complications)
                    Nerve, disease
                          (diabetic neuropathy; combined use of a GLP-1 compound and a modulator of diabetic late complications)
                      Eve. disease
                              (diabetic retinopathy; combined use of a GLP-I
                              compound and a modulator of diabetic late complications)
   IT Gene, animal Recurrence of the Competence of 
                                          mpound and a modulator of diabetic late complications)
                          (non-insulin-dependent; combined use of a GLP-1
                               compound and a modulator of diabetic late complications)
                    Antidiabetic agents
                  Drug delivery systems
```

```
$16968 IPCI A61K0038-00 [ICM,7]; A61K0031-138 [ICS,7]; A61K031-167 [ICS,7]; A61K0031-167 [ICS,7]; A61K0031-126 [ICS,7]; A61K0031-126 [ICS,7]; A61K0031-121 [ICS,7]; A61K0031-121 [ICS,7]; A61K0031-121 [ICS,7]; A61K0031-121 [ICS,7]; A61K0031-1403 [ICS,7]; A61K0031-1408 [ICS,7]; A61K0031-1418 [ICS,7]; A61K0031-1418 [ICS,7]; A61K0031-1418 [ICS,7]; A61K0031-1418 [ICS,7]; A61K0031-1418 [ICS,7]; A61K0031-1418 [ICS,7]; A61K0031-14196 [ICS,7]; A61K0031-1418 [ICS,7]; A61K0031-14196 [ICS,7]; A61K0031-157 [ICS,7]; A61K0031-157 [ICS,7]; A61K0031-157 [ICS,7]; A61K0031-570 [ICS,7]; A61F0003-10 [ICS,7]; A61F0031-10 [ICS,7]; A61K0031-10 [ICS,7]; A61F0031-10 [ICS,7]; A61
   JP 2005516968 IPCI A61K0038-00 [ICM,7]; A61K0031-138 [ICS,7]; A61K0031-165
                                                                 4C084/RA05; 4C084/RA06; 4C084/ZA021; 4C084/ZA262;
4C084/ZA331; 4C084/ZA361; 4C084/ZA421; 4C084/ZA422;
4C084/ZA811; 4C084/ZC202; 4C084/ZC351; 4C084/ZC422;
4C086/AA01; 4C086/AA02; 4C086/BC07; 4C086/BC10;
4C086/BC13; 4C086/BC30; 4C086/BC32; 4C086/BC38;
4C086/BC62; 4C086/BC5; 4C086/CB27;
4C086/BC407; 4C086/GA10; 4C086/GA12; 4C086/MA02;
4C086/MA04; 4C086/MA07; 4C086/MA52; 4C086/MA55;
                        (oral; combined use of a GLP-1 compound and a
modulator of diabetic late complications)
                Drug delivery systems
(parenterals; combined use of a GLP-1 compound and a
                modulator of diabetic late complications)
496765-91-4

IT 496765-91-4
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (amino acid sequence; combined use of a GLP-1 compound and a modulator of diabetic late complications)
IT 525-66-6, Propranolol 13523-86-9, Pindolol 26839-75-8, Timolol 29122-68-7, Atenolol 37517-30-9, Acebutolol 42200-33-9, Nadolol 51384-51-1, Metoprolol 62571-86-2, Captopril 75847-73-3, Enalapril 76547-98-3, Lisinopril 81147-92-4, Esmolol 83647-97-6, Spirapril 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 89371-37-9, Imidapril 89750-14-1D, GLP-1, analogos of fragments 98048-97-6, Fosinopril

            87679-37-6, Trandolapril 89371-37-9, Imidapril 89750-14-1D, GLP-1, analogs of fragments 98048-97-6, Fosinopril 107133-36-8, Perindopril erbumine 114798-26-4, Losartan 135038-57-2, Alatriopril 136087-85-9, Fidarestat 13782-25-3-4, Valsartan 138402-11-6, Irbesartan 141732-76-5, Exendin-4 141732-76-5D, Exendin-4, derivs. 169939-94-0, Ly 333531 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combined use of a GLP-1 compound and a modulator of diabetic late complications)
                        diabetic late complications)
             9015-82-1, Angiotensin-converting enzyme 9028-31-3, Aldose reductase 141436-78-4, Protein kinase C
             RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (inhibitors; combined use of a GLP-1 compound and a modulator of diabetic late complications)
 L33 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2003:320036 CAPLUS <<LOGINID::20070124>>
 DOCUMENT NUMBER:
                                                                                                                                               138-338498
                                                                       Preparation of human glucagon-like-peptide-1 mimics
and their use in the treatment of diabetes and related
 INVENTOR(S):
                                                                                                          Natarajan, Sesha I.; Bastos, Margarita M.;
Bernatowicz, Michael S.; Mapelli, Claudio; Lee, Ving; Ewing, William R.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 153 pp.
```

CODEN: PIXXD2

English

DOCUMENT TYPE:

LANGUAGE:

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. WO 2003033671 A2 20030424 WO 2002-US33386 A3 20051229 20021018 <--WO 2003033671 A2 20030424 WO 2002-US33386 20021018 ←WO 2003033671 A3 20051229

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, VY, UZ, AZ, MZ, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, EI, TJ, LU, MC, NI, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2463908 A1 20030424 CA 2002-2463908 20021018 ←JP 2005514337 T 20050519 JP 2003-536401 20021018
CN 1630709 A 20050622 CN 2002-820558 20021018
CN 1630709 A 20050622 CN 2002-820558 20021018
EF 1572892 A2 20050914 EP 2002-782185 20021018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
BR 2002013377 A 20060523 BR 2002-13377 20040323
ZA 2004002846 A 20050816 ZA 2004-2846 20040415
PRIORITY APPLN. INFO.: US 2001-342015P P 20011018

OTHER SOURCE(S): MARPAT 138:3338498

CTHER SOURCE(S): MARPAT 138:3338498

CTHER SOURCE(S): MARPAT 138:3338498

CTHER SOURCE(S): MARPAT 138:3338498 OTHER SOURCE(S): MARPAT 138:338498 AN 2003:320036 CAPLUS <<LOGINID::20070124>> ED Entered STN: 25 Apr 2003 TI Preparation of human glucagon-like-peptide-1 mimics and their use in the treatment of diabetes and related conditions IN Natarajan, Sesha I; Bastos, Margarita M.; Bernatowicz, Michael S.; Mapelli, Claudio; Lee, Ving; Ewing, William R. PA Bristol-Myers Squibb Company, USA SO PCT Int. Appl., 153 pp. CODEN: PIXXD2 DT Patent LA English IC ICM C12N CC 34-3 (Amino Acids, Peptides, and Proteins) Section cross-reference(s): 1, 63 FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE

[L,C*]; A61K0038-26 [L,A]; A61P0003-00 [L,C*];
A61P0003-04 [L,A]; A61P0003-36 [L,A]; A61P0003-10
[L,A]; A61P0005-00 [L,C*]; A61P0005-50 [L,A];
A61P0009-00 [L,C*]; A61P0009-10 [L,A]; A61P0009-12
[L,A]; A61P0013-00 [L,C*]; A61P0013-12 [L,A]; A61P0025-00
[L,C*]; A61P0013-00 [L,C*]; A61P0013-12 [L,A]; A61P0025-00
[L,C*]; A61P0025-00 [L,A]; A61P0017-00 [L,C*];
A61P0027-02 [L,A]; A61P0043-00 [L,C*]; A61P0043-00
[L,A]; C07K0007-00 [L,C*]; C07K0007-06 [L,A];
C07K0007-08 [L,A]; C07K0014-00 [L,C*]; C07K0014-00
[L,A]; C07K0014-435 [L,C*]; C07K0014-605 [L,A];

JP 2005514337 IPCI C07K0007-06 [ICM,7]; A61K0038-00 [ICS,7]; A61P0003-04
[ICS,7]; A61P0003-06 [ICS,7]; A61P0005-50 [ICS,7];
A61P0005-00 [ICS,7,C*]; A61P0009-10 [ICS,7,C*];
A61P0005-00 [ICS,7,C*]; A61P0009-10 [ICS,7,C*];
A61P0013-12 [ICS,7]; A61P0017-00 [ICS,7,C*];
A61P0013-12 [ICS,7]; A61P0017-00 [ICS,7,C*];
A61P0017-02 [ICS,7]; A61P0017-00 [ICS,7,C*];
A61P0013-12 [ICS,7]; A61P0017-00 [ICS,7];
C07K0007-00 [ICS,7,C*]; C07K0014-00 [ICS,7];

PCR, A61K0038-00 [N,A]; A61K0038-00 [N,C*]; C07K0014-435
[L,C*]; C07K0014-605 [I,A]

FTERM 4C084/AA02; 4C084/AA06; 4C084/AA07; 4C084/BA01; 4C084/BA03; 4C084/BA03;

```
PI WO 2003033671 A2 20030424 WO 2002-US33386 20021018 <--
WO 2003033671 A3 20051229
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CC, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NIL, PT, SE, SK, TB, BT, BJ, CF, CG, CI, CM, GA, GM, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2463908 A1 20030424 CA 2002-2463908 20021018 <--
IP 2003514337 T 20050519 JP 2003-536401 20021018
CN 1630709 A 20050622 CN 2002-820558 20021018
EP 1572892 A2 20050914 EP 2002-782185 20021018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NI, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
BR 2002013377 A 20060523 BR 2002-13377 20021018
NO 2004001203 A 20040610 NO 2004-1203 20040323
ZA 2004002846 A 20050816 ZA 2004-2846 20040415
PRAIUS 2001-34015P P 20011018
WO 2002-US33386 W 20021018
CLASS
PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES
WO 2003033671 ICM C12N
IPCR A61K0038-00 [LC*]; A61K0038-00 [LA]; A61K0038-26 [LC*]; A61P0009-00 [LC*]; A61P0009-00 [LC*]; A61P0009-10 [LA]; A61P0009-10 [LC*]; A61P0009-10 [LA]; A61P0009-10 [LC*]; A61P0009-00 [LC*]; A61P0009-10 [LA]; A61P0009-10 [LC*]; A61P0009-10 [LA]; A61P0009-10 [LA]; A61P0009-00 [LC*]; A61P0009-10 [LA]; A61P0009-10 [LC*]; A61P0009-00 [LC*]; C07K0014-00 [LC*]; A61K0038-06 [LCS,7];
```

```
EP 1572892 IPCI C12N0001-00 [ICM,7]

IPCR A61K0038-00 [L,C*]; A61K0038-00 [LA]; A61K0038-08

[LC]; A61K0038-06 [LA]; A61F0003-00 [LC*]; A61F0003-04

[LA]; A61F0003-06 [LA]; A61F0003-10 [LA]; A61P0003-04

[LA]; A61F0003-06 [LA]; A61F0003-10 [LA]; A61P0009-00

[LC*]; A61F0009-10 [LA]; A61F0003-10 [LA]; A61F0009-00

[LC*]; A61F0013-00 [LC*]; A61F0013-12 [LA]; A61F0017-00

[LC*]; A61F0017-02 [LA]; A61F0025-00 [LC*]; A61F0017-01

[LC*]; A61F0017-02 [LA]; A61F0043-00 [LC*]; A61F0027-02

[LA]; A61F0043-00 [LC*]; A61F0043-00 [LA]; C07K0007-00

[LC*]; C07K0007-06 [LA]; C07K007-08 [LA];

C07K0014-06 [LC*]; C07K0014-00 [LA]; C07K0014-435

[LC*]; C07K0014-605 [LA]

ECLA C07K014/605

BR 2002013377 IPCI A61K0038-00 [ICS,7]; A61K0038-08 [ICS,7]; C07K0002-00

[NA]; C07K0014-605 [LA]

ECLA C07K014/605

NO 2004001203 IPCI C07K0014-605 [ICM,7]; C07K0014-435 [ICM,7,C*];

C07K0004-00 [ICS,7]

IPCR A61K0038-10 [ICS,7]; A61K0038-00 [LA]; A61K0038-08

[ICS,7]; A61K0038-10 [ICS,7]; A61K0038-00 [LA]; A61K0038-08

[ICS,7]; A61K0038-10 [ICS,7]; A61K0038-00 [LA]; A61F0009-00 [LC*]; A61F0009-00 [LC*]; A61F0003-10

[LA]; A61F0003-00 [LC*]; A61F0003-10 [LA]; A61F0009-12

[LA]; A61F0003-00 [LC*]; A61F0003-10 [LA]; A61F0009-12

[LA]; A61F0013-00 [LC*]; A61F0003-10 [LA]; A61F0009-12

[LA]; C07K0014-05 [LA]; A61F0003-00 [LA]; A61F0003-00

[LA]; C07K0014-03 [LC*]; A61F0003-00 [LC*]; A61F0003-00

[LA]; C07K0014-05 [LC*]; A61F0003-00 [LC*]; A61F0003-00

[LA]; C07K0014-05 [LC*]; A61F0003-00 [LC*]; A61F0003-00

[LA]; C07K0014-05 [LC*]; C07K0014-05 [LA]; C07K0014-00

[LA]; C07K0014-05 [LC*]; C07K0014-05 [LA]; C07K0014-00

[LA]; C07K0014-05 [LC*]; C07K0014-05 [LA]; C07K0014-00

[LA]; C07K0014-05 [LA]; C07K0014-05 [LA]; C07K0014-00

[LA]; C07K0014-05 [LA]; C07K0014-05 [LA]; C07K0014-00

[LA]; C07K0014-05 [L
```

1-15 amino acid residues, an R group [H, (cyclo)alkyl, cycloalkylalkyl, heterocyclyl, heterocycloalkyl, (hetero)aryl, arylalkyl, aryloxyalkyl, heteroarylalkyl, or heteroaryloxyalkyl], an RCO (amide) group, a carbamate group, a urea, a sulfonamido, or an aminosulfonyl group; B is OH, alkoxy, etc., an amino or amino acid residue, or a peptide containing from 1-15 amino acid residues, terminating at the C-terminus as a carboxamide, ester, an amino part of the parties of the article of the parties. carboxyl, or an amino alc.] that mimic the biol. activity of the native GLP-1 peptide and thus are useful for the treatment or our perpendicular of the diseases of diseases of diseases associated with GLP activity. These chemical-modified peptides stimulate insulin secretion in type II diabetics and produce other beneficial insulinotropic responses, while exhibiting and produce other beneficial insulinotropic responses, while exhibiting increased stability to proteolytic cleavage making them ideal therapeutic candidates for oral or parenteral administration. A method of preparing the polypeptides comprises replacing the message sequence of the polypeptide with a variant message sequence capable of inducing receptor mediated signal transduction. An example is claimed peptide H-AEGTFTSD-Bip(2-Et)-Bip(2-Me)-NH2 (Bip = biphenylalanine residue).

ST glucagon like peptide mimic prepn treatment diabetes

IT Antiarteriosclerotics

(antiatherosclerotics; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

IT Kidney, disease

(diabetic nephropathy; preparation of human glucagon-like-peptide I mimics for use in treatment of diabetes and related conditions)

Nerve, disease

(diabetic neuropathy; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

(diabetic retinopathy; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

for use in treatment of diabetes and related conditi IT Metabolic disorders

(metabolic syndrome X; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

IT Antidiabetic agents

Antihypertensives

Antiobesity agents Atherosclerosis

Diabetes mellitus

Hyperglycemia

Hypertension Hypertriglyceridemia

Hypolipemic agents

Wound healing

(preparation of human glucagon-like-peptide-1 mimics for use in treatment of

```
$16520-74-4P $16520-75-5P $16520-77-7P $16520-79-9P $16520-81-3P $16520-82-4P $16520-84-6P $16520-86-8P $16520-87-9P $16520-89-1P $16520-91-7P $16520-93-7P $16520-93-7P $16521-03-2P $16521-03-4P $16521-03-4P $16521-03-4P $16521-03-4P $16521-03-4P $16521-03-4P $16521-13-4P $16521-13-4P $16521-13-4P $16521-12-5P $16521-13-4P $16521-12-5P $16521-13-4P $16521-12-5P $16521-13-4P $16521-23-4P $16521-23-4P $16521-33-4P $16521-33-4P $16521-33-4P $16521-33-4P $16521-33-4P $16521-33-4P $16521-34-3P $1652
                  RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (preparation of human glucagon-like-peptide-1 mimics for use in treatment of
diabetes and related conditions)
IT 150-46-9, Triethyl borate 1973-22-4, 1 Bromo 2 ethylbenzene 4326-36-7
16419-60-6, o Tolylboronic acid 93267-04-0 516521-49-6
                  RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)
                 90002-36-1P, 2 Ethylphenylboronic acid 112766-18-4P 516521-46-3P 516521-47-4P 516521-48-5P 516521-50-9P 516521-51-0P
                    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
                    (Reactant or reagent)
(Reactant or reagent)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

IT 51-64-9, Dexamphetamine 94-20-2, Chloropropamide 122-09-8, Phentermine 637-07-0, Clofibrate 657-24-9, Metformin 9004-10-8, Insulin, biological studies 1023-82-13, Glyburide 14838-15-4, Phenylpropanolamine 21187-98-4, Gliclazide 22232-71-9, Mazindol 25812-30-0, Gemfibrozii 29094-61-9, Glipizide 49562-28-9, Fenofibrate 6410-904, Aparbace 27432-03-2, Melikul 753-030-75-5, Lovastatin
```

25812-30-0, Gemfibrozil 29094-61-9, Glipizide 49562-28-9, Penofibrate 56180-94-0, Acarbose 72432-03-2, Miglitol 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 105816-04-4, Nateglinide 106650-56-0, Sibutramine 11025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 141750-63-2, Nisvastatin 141758-74-9, AC 2993 144288-97-1, TS-962 145599-86-6, Cerivastatin 152755-31-2, LV295427 159183-92-3, L750355 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 170861-63-9, JTT-501 176435-10-2, LV315902 178759-95-0, MD 700 196808-45-4 199113-98-9 199914-96-0, YM-440 213252-19-8, KPP297 244081-42-3, AJ9677 258345-41-4, GW-409544 262352-17-0, CP 529414 282526-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0,

```
KAD1129 335149-17-2, ARHO39242 335149-23-0, NVPDPP-728A 335149-25-
      CP331648 430433-17-3, Glipyride 444069-80-1, Axokine RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preparation of human glucagon-like-peptide-1 mimics for use in treatment of
           diabetes and related conditions)
 L33 ANSWER 5 OF 9 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
 ACCESSION NUMBER: 2003:390202 BIOSIS <<LOGINID::20070124>>
DOCUMENT NUMBER: PREV200300390202
                              The glucagon-like peptides: A double-edged therapeutic
sword?.
AUTHOR(S): Perry, TracyAnn [Reprint Author]; Greig, Nigel H.
CORPORATE SOURCE: Section of Drug Design and Development, Laboratory of
Neurosciences, Gerontology Research Center, National
Institute on Aging, National Institutes of Health, 5600
Nathan Shock Drive, Baltimore, MD, 21224, USA
perry@grc.nia.nih.gov
SOURCE: Trends in Pharmacological Science (Mile 2003)
                       sword?.
perryt@grc.nia.nih.gov

SOURCE: Trends in Pharmacological Sciences, (July 2003)

Vol. 24, No. 7, pp. 377-383. print.

ISSN: 0165-6147 (ISSN print).

DOCUMENT TYPE: Article

General Review; (Literature Review)

LANGUAGE: English

ENTRY NATE:
 LANGUAGE: English
ENTRY DATE: Entered STN: 27 Aug 2003
 Last Updated on STN: 27 Aug 2003
AN 2003:390202 BIOSIS <<LOGINID::20070124>>
 DN PREV200300390202
        The glucagon-like peptides: A double-edged therapeutic sword?.
AU Perry, TracyAnn [Reprint Author]; Greig, Nigel H.
CS Section of Drug Design and Development, Laboratory of Neurosciences,
Gerontology Research Center, National Institute on Aging, National
Institutes of Health, 5600 Nathan Shock Drive, Baltimore, MD, 21224, USA
      perryt@grc.nia.nih.gov
      o Trends in Pharmacological Sciences, (July 2003) Vol. 24, No. 7, pp. 377-383. print.
ISSN: 0165-6147 (ISSN print).
      General Review; (Literature Review)
 LA English
ED Entered STN: 27 Aug 2003
Last Updated on STN: 27 Aug 2003

AB Glucagon-like peptide-1(7-36)-amide (GLP-1) is an endogenous peptide that is secreted from the gut in response presence of food. Recent studies have established that GLP-
```

diabetes and related conditions)

diabetes and related conditions)

RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of human glucagon-like-peptide-1 mimics for use in treatment of

Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

(Uses)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

IT 89750-14-1DP, Glucagon-like peptide 1, mimics 516514-32-2P
516514-38-89 516514-43-5P 5165114-47-9P 516514-52-6P 516514-52-6P 516514-43-8P 516514-43-5P 516514-47-9P 516514-52-6P 516514-72-0P 516514-58-2P 516514-43-8P 516514-43-9P 516514-68-4P 516514-72-0P 516514-53-9P 516514-91-3P 516514-91-3P 516514-91-3P 516514-91-3P 516514-91-3P 516515-03-0P 516515-34-7P 516515-34-7P 516515-34-7P 516515-34-7P 516515-34-7P 516515-34-7P 516515-34-7P 516515-34-7P 516515-50-7P 516515-34-7P 516515-34-7P 516515-50-7P 516516-30-5P 516516-60-2P 516516-60-2P 516516-60-2P 516516-60-39-5P 516516-60-39-5P 516516-60-30-5P 516517-00-30-5P 516517-00-30-5P 516517-00-30-5P 516517-00-30-5P 516517-50-3P 516517-50-3P 516517-30-3P 516517-

IT Hyperlipidemia

I and its longer-acting analog exendin-4 have multiple synergistic effects on glucose-dependent, insulin secretion pathways of the pancreatic beta-cell and on plasticity in neuronal cells. Recent interest has focused on the development of these peptides as a novel therapeutic strategy for non-insulin-dependent (type 2) diabetes mellitus and associated neuropathy. This is with a view to developing lead corrapounds, based on neurotrophic action, for central and peripheral degenerative disorders such as stroke and Alzheimer's disease in addition to the peripheral neuropathy associated with type 2 diabetes mellitus. Here, we address recent advances in the biological action of GLP

Here, we address recent advances in the biological action of GLP

-1 and its related analogs.

CC Cytology - Animal 02506

Biochemistry studies - Proteins, peptides and amino acids 10064

Biochemistry studies - Carbohydrates 10068

Pathology - Therapy 12512

Metabolism - Metabolic disorders 13020

Cardiovascular system - Blood vessel pathology 14508 Endocrine - General 17002

Endocrine - Pancreas 17008
Endocrine - Pancreas 17008
Endocrine - Neuroendocrinology 17020
Nervous system - Physiology and biochemistry 20504
Nervous system - Pathology 20506
Pharmacology - General 22002

IT Major Concepts
Endocrine System (Chemical Coordination and Homeostasis); Nervous

System (Neural Coordination); Pharmacology IT Parts, Structures, & Systems of Organisms

beta cells: endocrine system; neuronal cells: nervous system

Alzheimer's disease: behavioral and mental disorders, nervous system

Alzheimer Disease (MeSH)

diabetic neuropathy; endocrine disease/pancreas, metabolic disease, nervous system disease

Diabetic Nephropathies (MeSH)

IT Diseases

stroke: nervous system disease, vascular disease Cerebrovascular Disorders (MeSH)

T Diseases

type 2 diabetes mellitus: endocrine disease/pancreas, metabolic disease

Diabetes Mellitus, Non-Insulin-Dependent (MeSH)

glucagon-like peptide-1(7-36)-amide; glucose; insulin IT Miscellaneous Descriptors

drug development

the patients, known duration of diabetes, metabolic control, BMI, or residual beta-cell pancreatic function. Endogenous creatinine clearance was significantly reduced under conditions of overt diabetic nephropathy, compared with normo and microalbuminuric patients nephropathy, compared with normo and nurconaluminum paneins (p<0.01). Uninary exercition of GLP-1 was significantly higher in normoalbuminum patients compared to controls (490.4+211.5 vs. 275.5+132.1 pg/min; p<0.05), with further increase under incipient diabetic nephropathy conditions (648.6+305 pg/min; p<0.01). No significant difference resulted, in contrast, between macroproteinuric patients and non-diabetic subjects. Taking all patients examined into account, a significant positive relationship emerged between urinary GLP-1 and creatinine clearance (p=0.04). In conclusion, an early tubular impairment in type 2 diabetes would occur before the onset of glomerular permeability alterations. The tubular dysfunction seems to evolve with the development of persistent microalbuminuria. Finally, the advanced tubular involvement, in terms of urinary GLP1 excretion, under overt diabetic nephropathy conditions would be masked by severe concomitant glomerular damage with the coexistence of both alterations resulting in a peptide excretion similar to control subjects.

Schemistry studies - Proteins, peptides and amino acids 10064
Metabolism - Metabolic disorders 13020
Urinary system - Pathology 15506
Endocrine - General 17002

Endocrine - Pancreas 17008 IT Major Concepts

Clinical Endocrinology (Human Medicine, Medical Sciences); Nephrology (Human Medicine, Medical Sciences)

diabetic nephropathy: endocrine disease/pancreas, metabolic

disease, urologic disease Diabetic Nephropathies (MeSH)

type 2 diabetes mellitus: endocrine disease/pancreas, metabolic disease, non-insulin-dependent diabetes mellitus Diabetes Mellitus, Non-Insulin-Dependent (MeSH)

IT Chemicals & Biochemicals

creatinine; glucagon-like peptide 1: renal tubular integrity indicator; glucagon-like peptide 1 7-36 amide [GLP-1 7-36

amide): urinary excretion

IT Miscellaneous Descriptor glomerular permeability ORGN Classifier

Super Taxa

Hominidae 86215

Primates; Mammalia; Vertebrata; Chordata; Animalia

```
RN 118549-37-4 (glucagon-like peptide-1(7-36)-amide)
        50-99-7Q (glucose)
58367-01-4Q (glucose)
        9004-10-8 (insulin)
 L33 ANSWER 6 OF 9 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
       DUPLICATE I
ACCESSION NUMBER: 2001:506591 BIOSIS <<LOGINID::20070124>> DOCUMENT NUMBER: PREV200100506591
                               Urinary excretion of glucagon-like peptide 1 (GLP
-1) 7-36 amide in human type 2
-1) 1-30 amide in human type 2
(non-insulin-dependent) diabetes mellitus.

AUTHOR(S): Lugari, R. [Reprint author]; Ugolotti, D.; Dei Cas, A.;

Barilli, A. L.; lotti, M.; Marani, B.; Orlandini, A.;

Gnudi, A.; Zandomeneghi, R.

CORPORATE SOURCE: Cattedra di Endocrinologia, Via Gramsci 14, 43100, Parma,
Italy
endoparm@iprumiv.cce.unipr.it

SOURCE: Hormone and Metabolic Research, (September, 2001)
Vol. 33, No. 9, pp. 568-571, print.
CODEN: HMMRA2. ISSN: 0018-5043.

DOCUMENT TYPE: Article

LANGUAGE: English
ENTRY DATE: Entered STN: 31 Oct 2001

Last Updated on STN: 23 Feb 2002

AN 2001:506591 BIOSIS <<LOGINID::20070124>>
DN PREV200100506591

I. Ultimary expertion of glues googalike pertide 1 (GI Pal)
DN PREV200100506591
Tl Urinary excretion of glucagon-like peptide 1 (GLP-1)
7-36 amide in human type 2 (non-insulin-dependent) diabetes mellitus.
AU Lugari, R. (Reprint author); Ugolotti, D.; Dei Cas, A.; Barilli, A. L.;
lotti, M.; Marani, B.; Orlandini, A.; Gnudi, A.; Zandomeneghi, R.
CS Cattedra di Endocrinologia, Via Gramsci 14, 43100, Parma, Italy
endoparm@ipruniv.cce.unipr.it
SO Hormone and Metabolic Research, (September, 2001) Vol. 33, No.
9, pp. 568-571. print.
CODEN: HMMRA2. ISSN: 0018-5043.
DT Article
 DT Article
LA English
 ED Entered STN: 31 Oct 2001
Last Updated on STN: 23 Feb 2002
 AB The urinary excretion of insulinotropic glucagon-like peptide 1 (
GLP-1) was investigated as an indicator of renal tubular
       integrity in 10 healthy subjects and in 3 groups of type 2 diabetic patients with different degrees of urinary albumin excretion rate. No
        significant difference emerged between the groups with respect to age of
```

```
Organism Name
           human: patient
       Taxa Notes
             Animals, Chordates, Humans, Mammals, Primates, Vertebrates
 RN 60-27-5 (creatinine)
 L33 ANSWER 7 OF 9 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights
 reserved on STN
ACCESSION NUMBER: 96034762 EMBASE <<LOGINID::20070124>>
 ACCESSION NUMBER: 96034/62 EMBASE < LOCINID::200/0124
DOCUMENT NUMBER: 1996034762
TITLE: Gastric emptying, glucose responses, and insulin secretion after a liquid test meal: Effects of exogenous glucagon-like peptide-1 (GLP-1)-(7-36) amide in type 2 (noninsulin-dependent) diabetic patients.

AUTHOR: Willins B.; Werner J.; Holst J.J.; Orskov C.; Creutzfeldt
                            W : Nauck M.A.
 CORPORATE SOURCE: Department of Medicine, Ruhr-University Bochum,
Knappschafts-Krankenhaus, In der Schornau 23-25,44892
Bochum, Germany
SOURCE: Journal of Clinical Endocrinology and Metabolism, (
                            1996) Vol. 81, No. 1, pp. 327-332. .
ISSN: 0021-972X CODEN: JCEMAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
037 Drug Literature Index
English
SIMMANUS
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 1996
Last Updated on STN: 20 Feb 1996
AN 96034762 EMBASE <<LOGINID::20070124>>
  DN 1996034762
 DN 1990039 02.

TI Gastric emptying, glucose responses, and insulin secretion after a liquid test meal: Effects of exogenous glucagon-like peptide-1 (GLP-1)-(7-36) amide in type 2 (noninsulin-dependent) diabetic
17(7-30) annue in type 2 (noninstant-appendent) diabetic patients.

AU Willms B.; Werner J.; Holst J.J.; Orskov C.; Creutzfeldt W.; Nauck M.A.

CS Department of Medicine, Ruhr-University Bochum, Knappschafts-Krankenhaus, In der Schormau 23-25,44892 Bochum, Germany

SO Journal of Clinical Endocrinology and Metabolism. (1996) Vol.
```

81, No. 1, pp. 327-332. . ISSN: 0021-972X CODEN: JCEMAZ

037 Drug Literature Index

CY United States DT Journal; Article FS 003 Endocrinology

```
SL English
 ED Entered STN: 20 Feb 1996
Last Updated on STN: 20 Feb 1996

AB The aim of the study was to investigate whether inhibition of gastric emptying of meals plays a role in the mechanism of the blood
           emptying of meals plays a role in the mechanism of the blood glucose-lowering action of glucagon-like peptide-1-(7-36) amide [ GLP-1-(7-36) amide] in type 2 diabetes. Eight poorly controlled type 2 diabetic patients (age, 58\pm6 yr; body mass index, 30.0\pm5.2 kg/m<sup>2</sup>; hemoglobin A(1c), 10.5\pm1.2\%) were studied in the fasting state (plasma glucose, 11.1\pm1.1 mmol/L). A liquid meal of 400 mL containing 8% amino acids and 50 g sucrose (327 Kcal) was administered at time zero by a nasogastric tube. Gastric volume was determined by a dive dilution technique using phenol ged. In randomize
          administered at time zero by a nasogastric tube. Gastric volume was determined by a dye dilution technique using phenol red. In randomized order, GLP-1-(7-36) amide (1.2 pmol/kg·min; Saxon Biochemicals) or placebo (0.9% NaCl with 1% human serum albumin) was infused between -30 and 240 min. In the control experiment, gastric emptying was completed within 120 min, and plasma glucose, insulin, C-peptide, GLP-1-(7-36) amide, and glucagon concentrations transiently increased. With exogenous GLP-1-(7-36) amide, and glucagon concentrations transiently increased. With exogenous GLP-1-(7-36) amide, and glucagon concentrations transiently increased.
          concentrations transiently increased. With exogenous GLP-1-(7-36) amide (plasma level, apprx.70 pmoVL), gastric volume remained constant over the period it was measured (120 min; P < 0.0001 vs. placebo), and plasma glucose fell to normal fasting values (5.4 \pm 0.7 mmoVL) within 3-4 h, whereas insulin was stimulated in most, but not all, patients, and glucagon remained at the basal level or was slightly suppressed. In conclusion, GLP-1-(7-36) amide inhibits gastric emptying in type 2 diabetic patients. Together with the stimulation of insulin and the inhibition of glucagon secretion, this effect probably contributes to the blood glucose-lowering action of GLP-1-(7-36) amide in two 2-diabetic patients when
            GLP-1-(7-36) amide in type 2-diabetic patients when studied after meal ingestion. At the degree observed, inhibition of
            gastric emptying, however, must be overcome by tachyphylaxis, reduction in dose, or pharmacological interventions so as not to interfere with the therapeutic use of GLP-1-(7-36) amide in type 2
diabetic patients.

CT Medical Descriptors:
              *insulin release
*non insulin dependent diabetes mellitus: DT, drug therapy
               *non insulin dependent diabetes mellitus: TH, therapy
                stomach emptying
            thibs
            aged
              article
              clinical article
            clinical trial
```

LA English

controlled study

```
heterotopic pancreas and kidney transplantation.

AUTHOR(S): Nauck, M. A. [Reprint author]; Buesing, M.; Orskov, C.; Siegel, E. G.; Talartschik, J.; Baartz, A.; Baartz, T.; Hopt, U. T.; Becker, H.-D.; Creutzfeld, W.

CORPORATE SOURCE: Div. Gastroenterol. and Endocrinol., Dep. Med., Georg August Univ., Robert-Koch-Strasse 40, W-3400 Goettingen, Germany

SOURCE: Acta Diabetologica, (1993) Vol. 30, No. 1, pp. 39-45.

CODEN: ACDAEZ. ISSN: 0940-5429.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 8 Sep 1993

Last Updated on STN: 3 Jan 1995

AN 1993-4605694 BIOSIS <<LOGINID::20070124>>

DN PREV199396074419

TI Preserved incretin effect in type 1 diabetic patients with end-stage nephropathy treated by combined heterotopic pancreas and kidney transplantation.

AU Nauck, M. A. [Reprint author]; Buesing, M.; Orskov, C.; Siegel, E. G.; Talartschik, J.; Baartz, A.; Baartz, T.; Hopt, U. T.; Becker, H.-D.; Creutzfeldt, W.

CS Div. Gastroenterol. and Endocrinol., Dep. Med., Georg August Univ., Robert-Koch-Strasse 40, W-3400 Goettingen, Germany

SO Acta Diabetologica, (1993) Vol. 30, No. 1, pp. 39-45.

CODEN: ACDAEZ. ISSN: 0940-5429.

DT Article

LA English

ED Entered STN: 8 Sep 1993

Last Updated on STN: 3 Jan 1995

Als Insulin secretion is stimulated better by oral than by intravenous glucose (incretin effect). The contribution of the autonomic nervous system to the incretin effect after oral glucose in humans is unclear. We therefore examined nine type 1 diabetic (insulin-dependent) patients with end-stage nephropathy, studied after combined heterotopic pancreas and kidney transplantation, and 7 non-diabetic kidney recipients (matched for creatinine clearance and immunosuppressive medication). The release of gastric inhibitory polypeptide (GIP) and glucagon-like peptide 1 (GIP-1) immunoraectivity and B cell secretory responses (IR insulin and C-peptide) to oral (50 g) and "isoglycaemic" intravenous glucose (IR insulin and C-peptide) to oral (50 g) and "isoglycaemic" intravenous (IR Deptide) to oral (5
```

glucose (identical glycaemic profile) were measured by radioimmunoassay. The difference in B cell responses between the two tests represents the

were similar in the two patient groups despite systemic venous drainage of the pancreas graft in the pancreas-kidney-transplanted group. In both

contribution of the enteroinsular axis to the response after oral glucose (incretin effect). Insulin responses after the oral glucose challenge

```
diabetic angiopathy: CO, complication
      diabetic nephropathy: CO, complication diabetic neuropathy: CO, complication
      diabetic retinopathy
      drug effect
      drug mechanism
     glucagon release
      glucose blood level
      hormone inhibition
     human
      hypertension: DT, drug therapy
     intravenous drug administration
     postprandial state
     priority journal
randomized controlled trial
     Drug Descriptors:

*glucagon like peptide 1 [7-36] amide: CM, drug comparison
      glucagon like peptide 1 [7-36] amide: DT, drug therapy 
*glucagon like peptide 1 [7-36] amide: DT, drug therapy 
*glucagon like peptide 1 [7-36] amide: PD, pharmacology 
*glucagon like peptide 1 [7-36] amide: CT, clinical trial 
*glucage: EC, endogenous compound 
*insulin: EC, endogenous compound
     acarbose: DT, drug therapy
captopril plus hydrochlorothiazide: DT, drug therapy
     glibenclamide: DT, drug therapy
isosorbide dinitrate: DT, drug therapy
metformin: DT, drug therapy
metoprolol: DT, drug therapy
metoprotoi: DT, drug therapy
nifedipine: DT, drug therapy
placebo: CM, drug comparison
RN (glucagon like peptide 1 [7-36] amide) 119637-73-9; (glucose) 50-99-7.
84778-642; (insulin) 9004-10-8; (acarbose) 56180-94-0; (glibenclamide)
10238-21-8; (isosorbide dinitrate) 87-33-2; (metformin) 1115-70-4,
657-24-9; (metoprolol) 37350-58-6; (nifedipine) 21829-25-4
CO Saxon (Germany)
L33 ANSWER 8 OF 9 BIOSIS COPYRIGHT (c) 2007 The Thornson Corporation on
STN
     DUPLICATE 2
ACCESSION NUMBER: 1993:408694 BIOSIS <<LOGINID::20070124>>
DOCUMENT NUMBER: PREV199396074419
TITLE: Preserved incretin effect in type 1 diabetic patients with
                      end-stage nephropathy treated by combined
```

```
groups GIP and GLP-1 increased after oral but not
         after intravenous glucose, and B cell secretory responses were significantly smaller (by 55.2 + 7.7% and 46.5 + 12.5%, respectively) with "isoglycaemic" intravenous glucose infusions. The lack of reduction in the incretin effect in pancreas-kidney-transplanted patients, whose functioning pancreas is denervated, indicates a lesser role for the
in the increan elect in paincreas-kinney-transplanted patients, whose functioning pancreas is denervated, indicates a lesser role for the nervous system and a more important contribution of circulating incretin hormones in mediating the enteroinsular axis in man.

CC Biochemistry studies - Proteins, peptides and amino acids 10064 Biochemistry studies - Carbohydrates 10068 Anatomy and Histology - Surgery 11105 Anatomy and Histology - Regeneration and transplantation 11107 Pathology - Therapy 12512 Metabolism - Carbohydrates 13004 Metabolism - Proteins, peptides and amino acids 13012 Metabolism - Proteins, peptides and amino acids 13012 Metabolism - Metabolic disorders 13020 Digestive system - Pathology 14006 Urinary system - Peneral and methods 14001 Digestive system - General and methods 15501 Urinary system - General and methods 15501 Urinary system - Pathology 15506 Endocrine - Pancreas 17008

IT Major Concepts Endocrine System (Chemical Coordination and Homeostasis);
               Major Concepts

Endocrine System (Chemical Coordination and Homeostasis);

Gastroenterology (Human Medicine, Medical Sciences); Metabolism;
                Physiology; Surgery (Medical Sciences); Urology (Hur
                Medical Sciences)
 IT Chemicals & Biochemicals
INCRETIN; GLUCAGON; INSULIN
.. INTEGRATIONS DESCRIPTORS
ANTIDIABETIC-DRUG; DIABETIC NEUROPATHY; ENZYME INHIBITOR-DRUG
  ORGN Classifier
              Hominidae 86215
          Super Taxa
                Primates; Mammalia; Vertebrata; Chordata; Animalia
          Organism Name
Hominidae
          Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 54241-84-8 (INCRETIN)
         9007-92-5 (GLUCAGON)
9004-10-8 (INSULIN)
 L33 ANSWER 9 OF 9 MEDLINE on STN
ACCESSION NUMBER: 92288534 MEDLINE <<LOGINID::20070124>>
DOCUMENT NUMBER: PubMed ID: 1600330
```

```
gastrointestinal hormone concentrations in type-1-diabetic patients after successful combined pancreas and kidney
 AUTHOR: Nauck M A; Busing M; Orskov C; Siegel E G; Talartschik J;
Baartz A; Baartz T; Holzer H; Hopt U T; Ebert R; +
CORPORATE SOURCE: Abteilung Gastroenterologie und Endokrinologie,
                         Georg-August-Universitat, Gottingen.
The Clinical investigator, (1992 Jan) Vol. 70,
GERMANY: Germany, Federal Republic of Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: ENTRY MONTH: 199207
ENTRY DATE: 199207
 No. 1, pp. 40-8.

Journal code: 9207154. ISSN: 0941-0198.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 ENTRY DATE: Entered $110: 24 Jul 1992
Last Updated on $TN: 24 Jul 1992
Entered Medline: 13 Jul 1992
AN 92288534 MEDLINE <<LOGINID::20070124>>
DN PubMed ID: 1600330
   TI Basal and nutrient-stimulated pancreatic and gastrointestinal hormone
        concentrations in type-1-diabetic patients after successful combined
 contentration in type-1-value patterns and sales successful contentration pancreas and kidney transplantation.

AU Nauck M A; Busing M; Orskov C; Siegel E G; Talartschik J; Baartz A; Baartz T; Holzer H; Hopt U T; Ebert R; + CS _Abteilung Gastroenterologie und Endokrinologie, Georg-August-Universitat,
 Gottingen.
SO The Clinical investigator, (1992 Jan) Vol. 70, No. 1, pp. 40-8.
Journal code: 9207154. ISSN: 0941-0198.
 CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
  LA English
  FS Priority Journals
 EM 199207
ED Entered STN: 24 Jul 1992
       Last Updated on STN: 24 Jul 1992
Entered Medline: 13 Jul 1992
  AB The secretion of pancreatic and gastrointestinal hormones in the basal
       state and after nutrient stimuli (50 g glucose, 50 g protein, or 30 g triglyceride administered on separate occasions) was assessed in ten previously type-1-diabetic patients after successful combined kidney and pancreas transplantation (systemic venous drainage). Pasting values were
       compared to matched non-diabetic kidney-transplanted patients and related to kidney function (endogenous creatinine clearance) and to the type and
        dosage of immunosuppressive medication. In the fasting state, only IR
```

Basal and nutrient-stimulated pancreatic and

TITLE:

PATENT ASSIGNEE(S): USA SOURCE: U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 273,975. CODEN: USXXCO DOCUMENT TYPE: Patent LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE US 2004127423 A1 20040701 US 2003-419399 A1 20031016 US 2002-273975 20030421 | No. WO 2004094461 A2 20060118 EP 2004-760098 20040421 EP 1615653 A2 20060118 EP 2004-760098 20040421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
PRIORITY APPLN. INFO.:
US 2001-342015P P 20011018
US 2002-273975 A2 20021018
US 2003-419399 A 20030421
WO 2004-US12374 W 20040421
AN 2004:533962 CAPLUS <<LOGINID::20070124>> DN 141:82335 ED Entered STN: 02 Jul 2004 TI Human glucagon-like-peptide-1 mimics and their antidiabetic effects
IN Natarajan, Sesha Iyer, Mapelli, Claudio; Bastos, Margarita M.;
Bernatowicz, Michael; Lee, Ving; Ewing, William R.

SO U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 273,975. CODEN: USXXCO

DT Patent

LA English IC ICM A61K038-10 ICS C07K007-08

insulin concentrations were higher in pancreas-kidney-transplanted insulin concentrations were higher in pancreas-kidney-transplanted patients (by 88%; P = 0.001) than in the kidney graft recipients. There were significant inverse correlations of plasma C-peptide, GIP, and gastrin immunoreactivity to endogenous creatinine clearance (kidney function). In response to nutrients, insulin secretion (IR insulin, C-peptide) was significantly stimulated by glucose, and - to a lesser degree - also by protein. Pancreatic glucagon was suppressed by glucos and stimulated by protein ingestion. GIP was raised after glucose and triglyceride more than after protein (P = 0.0003). GLP-1 immunoreactivity was stimulated by all nutrients, with a tendency towards higher responses to protein and fat (P = 0.00). Gastri Infinition that was stimmed up an indirect, who are tendency towards higher responses to protein and fat (P = 0.06). Gastrin was mainly raised by protein. In conclusion, the overall pattern of pancreatic and gastrointestinal hormone release is normal in patients after combined pancreas-kidney-transplantation, but there are some peculiarities due to (a) systemic venous drainage of the pancreas graft (elevated fasting IR insulin) and (b) impaired kidney function (negative correlation of fasting plasma values to endogenous creatinine clearance for C-peptide, GIP, and gastrin).(ABSTRACT TRUNCATED AT 250 WORDS) CT Check Tags: Female; Male Adult Blood Glucose: ME, metabolism

Diabetes Mellitus, Type 1: BL, blood
Diabetes Mellitus, Type 1: BL, blood
Diabetes Mellitus, Type 1: SU, surgery
Diabetic Nephropathies: BL, blood
Diabetic Nephropathies: SU, surgery *Gastrointestinal Hormones: BL, blood Kidney Function Tests *Kidney Transplantation: PH, physiology Middle Aged *Pancreas Transplantation: PH, physiology Pancreatic Function Tests

*Pancreatic Hormones: BL, blood Research Support, Non-U.S. Gov't CN 0 (Blood Glucose); 0 (Gastrointestinal Hormones); 0 (Pancreatic Hormones)

D Ibib all L34 1-9

L34 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN 2004:533962 CAPLUS <<LOGINID::20070124>> 141:82335 ACCESSION NUMBER: DOCUMENT NUMBER: Human glucagon-like-peptide-1 mimics and their antidiabetic effects

INVENTOR(S): Natarajan, Sesha Iyer, Mapelli, Claudio; Bastos, Margarita M.; Bernatowicz, Michael; Lee, Ving; Ewing, William R.

INCL 514015000; 530328000 CC 1-10 (Pharmacology) Section cross-reference(s): 2, 34, 63 FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. PI US 2004127423 A1 20040701 US 2003-419399 20030421 US 2003 195 157 WO 2004094461 WO 2004094461 I.U., I.G EP 1615653 A2 20060118 EP 2004-760098 20040421 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR PRAI US 2001-342015P P 20011018 US 2002-273975 A2 20021018 US 2003-419399 A 20030421 WO 2004-US12374 W 20040421 PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES US 2004127423 ICM A61K038-10 ICS C07K007-08 INCL 514015000; 530328000 PCI A61K0038-10 [ICM,7]; C07K0007-08 [ICS,7]; C07K0007-00 [ICS,7,C*] [ICS,7,C*]

IPCR A61K0038-00 [N,C*]; A61K0038-00 [N,A]; C07K0014-435

[I,C*]; C07K0014-605 [I,A]

NCL 514/015.000; 530/328.000

ECLA C07K014/605

US 2003195157 IPCI A61K0038-10 [ICM,7]; A61K0038-08 [ICS,7]; C07K0007-08

[ICS,7]; C07K0007-06 [ICS,7]; C07K0007-00 [ICS,7,C*]

IPCR A61K0038-00 [N,C*]; A61K0038-00 [N,A]; C07K0014-435

[LC*]; C07K0014-605 [LA] NCL 514/016.000; 514/017.000; 530/328.000; 530/329.000

ECLA C07K014/605

```
effects)
                                                                                                                                                                     Proteins
                                                                                                                                                                    RL: BSU (Biological study, unclassified); BIOL (Biological study)
                                                                                                                                                                      (cholesterol ester-exchanging; human glucagon-like-peptide-1
                                                                                                                                                                       their antidiabetic effects)
                                                                                                                                                                      (diabetic nephropathy; human glucagon-like-peptide-1 mimics
                                                                                                                                                                       and their antidiabetic effects)
                                                                                                                                                                     Nerve, disease
             [ICS,7,C*]
IPCR A61K0038-00 [LC*]; A61K0038-00 [LA]; A61K0038-02
                                                                                                                                                                      (diabetic neuropathy; human glucagon-like-peptide-1 mimics and their
                                                                                                                                                                      antidiabetic effects)
                 [LA]; C07K(0038-02 [LA]; A61K0038-03 [LA]; A61K0038-03 [LA]; A61K0038-03 [LA]; A61K0038-03 [LA]; A61K0038-10 [LC*]; A61K0038-10 [LC*]; A61K0038-10 [LA]; C07K(007-04 [LA]; C07K007-05 [LA]; C07K007-04 [LA]; C07K007-08 [LA]
                                                                                                                                                                     Eye, disease
                                                                                                                                                                      (diabetic retin
                                                                                                                                                                                       nopathy; human glucagon-like-peptide-1 mimics and their
                                                                                                                                                                       antidiabetic effects)
                                                                                                                                                                     Transport proteins
                                                                                                                                                                   RL: BSU (Biological study, unclassified); BIOL (Biological study)
AB The invention discloses human glucagon-like peptide-1 (GLP-1) peptide mimics that mimic the biol. activity of the native
                                                                                                                                                                     (dopamine transporter, human glucagon-like-peptide-1 mimics and their antidiabetic effects)
   GLP-1 peptide and thus are useful for the treatment or prevention of diseases or disorders associated with GLP activity. Further,
                                                                                                                                                                IT 5-HT reuptake inhi
    the invention provides novel, chemical modified peptides that not only
                                                                                                                                                                   Antihypertensives
   stimulate insulin secretion in type II diabetics, but also produce other
beneficial insulinotropic responses. These synthetic peptide GLP
                                                                                                                                                                    Antiobesity agents
                                                                                                                                                                    Appetite depressants
   -1 mimics exhibit increased stability to proteolytic cleavage
making them ideal therapeutic candidates for oral or parentera
                                                                                                                                                                    A themselerosis
                                                                                                                                                                     Diabetes mellitus
    administration.
                                                                                                                                                                    Human
                                                                                                                                                                    Hyperglycemia
ST human glucagon peptide mimic prepn diabetes antidiabetic insulin
                                                                                                                                                                     Hypertension
                                                                                                                                                                   Hypertriglyceridemia
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
                                                                                                                                                                    Hypolipemic agents
   (Biological study); USES (Uses)

(ALBP (adipocyte lipid-binding protein); human glucagon-like-peptide-l mimics and their antidiabetic effects)
                                                                                                                                                                    Signal transduction, biological
                                                                                                                                                                    Wound healing
                                                                                                                                                                   b3-Adrenoceptor ago
IT Lipoprotein receptors
   RL: BSU (Biological study, unclassified); BIOL (Biological study) (LDL; human glucagon-like-peptide-1 mimics and their antidiabetic
                                                                                                                                                                     (human glucagon-like-peptide-1 mimics and their antidiabetic effects)
Fatty acids, biological studies
                                                                                                                                                                   Glucagon-like peptide-1 receptors
Hyperlipidemia
      effects)
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
                                                                                                                                                                    Thyroid hormone receptors
    (Biological study); USES (Uses)
                                                                                                                                                                   RL: BSU (Biological study, unclassified); BIOL (Biological study)
    (MTP (microsomal triglyceride-exchanging protein), inhibitors; human glucagon-like-peptide-1 mimics and their antidiabetic effects)
Antiarteriosclerotics
                                                                                                                                                                      (human glucagon-like-peptide-1 mimics and their antidiabetic effects)
                                                                                                                                                                TP Peptides, biological studies
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
      (antiatherosclerotics; human glucagon-like-peptide-1 mimics and their
      antidiabetic effects)
                                                                                                                                                                      (human glucagon-like-pentide-1 mimics and their antidiabetic effects)
IT Drug delivery systems
                                                                                                                                                                IT Sulfonylureas
     (capsules; human glucagon-like-peptide-1 mimics and their antidiabetic
```

(Biological study); USES (Uses) (human glucagon-like-peptide-1 mimics and their antidiabetic effects) (Biological study), South (human glucagon-like-peptide-1 mimics and their antidiabeti IT Drug delivery systems (injections; human glucagon-like-peptide-1 mimics and their antidiabetic effects) (metabolic syndrome X; human glucagon-like-peptide-1 mimics and their antidiabetic effects) Drug delivery systems (microparticles; human glucagon-like-peptide-1 mimics and their intidiabetic effects) IT Diabetes mellitus (non-insulin-dependent; human glucagon-like-peptide-1 mimics and their antidiabetic effects) Antidiabetic agents Drug delivery systems (oral; human glucagon-like-peptide-1 mimics and their antidiabetic IT Drug delivery systems (suspensions; human glucagon-like-peptide-1 mimics and their antidiabetic effects) Drug delivery systems (tablets; human glucagon-like-peptide-1 mimics and their antidiabetic effects) IT Peroxisome proliferator-activated receptors RL: BSU (Biological study, unclassified); BIOL (Biological study)
(a; human glucagon-like-peptide-1 mimics and their antidiabetic IT Peroxisome proliferator-activated receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (g; human glucagon-like-peptide-1 mimics and their antidiabetic effects) IT 51-61-6, Dopamine, biological studies 56-81-5, Glycerol, biological studies 9001-62-1, Lipase 9028-35-7, 3-Hydroxy-3-methylglutaryl CoA reductase 9029-60-1, Lipoxygenase 9033-06-1, Glucosidase 9077-14-9, Squalene synthetase 63551-74-6, Lipoxygenase 90002-36-1, 2-Ethylphenyl RL: BSU (Biological study, unclassified); BIOL (Biological study) | Characteristics | Characteri

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

```
$16515-46-1P $16515-50-7P $16515-52-P $16515-59-6P $16515-63-2P $16515-68-7P $16515-68-7P $16515-68-7P $16515-68-7P $16515-68-7P $16515-68-7P $16515-88-1P $16515-92-7P $16515-96-1P $16516-60-66 $16516-10-2P $16516-14-6P $16516-18-0P $16516-61-1P $16516-06-60 $16516-10-2P $16516-14-6P $16516-18-0P $16516-62-2-6P $16516-26-0P $16516-17-P $16516-13-1P $16516-18-0P $16516-62-6P $16516-62-6P $16516-65-5P $16516-60-2P $16516-60-6P $16516-68-0P $16516-68-0P $16516-68-0P $16516-69-3P $16516-69-3P $16516-69-8P $16517-09-5P $16517-69-3P $16516-98-8P $16517-09-2P $16517-08-3P $16517-09-3P $16517-09-3P $16517-17-2P $16517-17-2P $16517-29-P $16517-25-P $16517-30-3P $16517-31-2P $16518-31-3P $16518-30-2P $16518-30-3P $16519-30-3P $16520-31-3P $16520-
```

```
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (human glucagon-like-peptide-1 mimics and their antidiabetic effects) IT 51-64-9, Dexamphet-amine 56-03-1, Biguanide 94-20-2, Chloropropamide 122-09-8, Phentermine 637-07-0, Clofibrate 657-24-9, Metformin 943-45-3D, Fibric acid, derivs. 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 21187-98-4, Gliclazide 2232-27-19, Mazindol 25812-30-0, Gemfübrozil 29094-61-9, Glipizide 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 56180-94-0, Acarbose 72432-03-2, Miglitol 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 89750-14-1, Glucagon-like peptide 1 93479-97-1, Glimepiride 39357-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 134523-00-5, Ator-vastatin 13502-62-1, Repaglinide 141750-63-2, Nisvastatin 141758-74-9, AC2993 144288-97-1, TS-962 145599-86-6, Cerivastatin 152755-31-2, LV295427 159183-92-3, L750355 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 170861-613-9, JTT-501 176435-10-2, LV315902 178759-95-0, MD 700 196808-45-4 199113-98-9, NN-2344 199914-96-0, YM-440 213252-17-0, CP 529414 282525-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-13-2, CP 31648 430433-17-3, Glipyride 444069-80-1, Axokine RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (human glucagon-like-peptide-1 mimics and their antidiabetic effects) IT 150-46-9, Trichylborate 358-23-6, Triftic anhydride 1973-22-4, 1-Bromo-2-ethylbenzene 4326-367 16419-60-6, O-Tolybboronic acid 32911-69-1 93267-04-0 516521-49-6 713497-86-0 RL: RCT (Reactant); RACT (Reactant or reagent) (human glucagon-like-peptide-1 mimics and their antidiabetic effects) IT 112766-18-4P 516521-46-3P 516521-47-4P 516521-48-5P 516521-50-9P 516521-51-0P RL: RCT
```

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; human glucagon-like-peptide-1 mimics and their antidiabetic effects)

IT 54249-88-6, Dipeptidyl peptidase IV

```
IN Daisy, Joe
PA Pfizer Products Inc., USA
SO Eur. Pat. Appl., 71 pp.
CODEN: EPXXDW
IC ICM C07D495-04
    ICS C07D491-04; C07D209-52; A61K031-407; A61P003-10; A61P009-10; C07D495-14; C07D333-00; C07D209-00; C07D307-00
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 2
    PATENT NO.
                                      KIND DATE APPLICATION NO. DATE
         P 1391460 A1 20040225 EP 2003-20676 20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
PI EP 1391460
             IE, FL CY
                                    A2 20010404 EP 2000-308131
                                   A3 20010627
     EP 1088824
        P 1088824 A3 20040107
P: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU
E, SI, LT, LV, FI, RO
US 2002183369 A1 20021205 US 2002-117370
US 6576653 B2 20030610
US 2003195361 A1 20031016 US 2003-367002
US 6828343 B2 20041207
PRAI US 1999-157148P P 19990930
EP 2000-308131 A3 20000918
US 2000-670759 A3 20000927
US 2002-117370 A3 20020405
                                                                                                         20020405 <--
                                                                                                         20030214 <--
CLASS
 PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES
EP 1391460 ICM C07D495-04
ICS C07D491-04; C07D209-52; A61K031-407; A61P003-10;
A61P009-10; C07D495-14; C07D333-00; C07D209-00;
                       C07D307-00
                       CO/D307-00

CO/D307-04

[ICS,7,C*]; C07D0491-04

[ICS,7,C*]; C07D0209-52

[ICS,7]; A61K0031-407

[ICS,7]; A61P0003-10

[ICS,7]; A61P0009-10

[ICS,7]; A61P0009-10

[ICS,7]; A61P0009-10

[ICS,7]; A61P0009-10

[ICS,7,C*];

C07D0495-14

[ICS,7]; C07D0495-00

[ICS,7,C*];

C07D0333-00

[ICS,7]; C07D0209-00

[ICS,7]; C07D0307-00
```

ECLA C07D491/04+307B+209B; C07D495/04+333B+209B;

```
(inhibitors; human glucagon-like-peptide-1 mimics and their
antidiabetic effects)

17 9004-10-8, Insulin, biological studies
   RL: BSU (Biological study, unclassified); BIOL (Biological study) (resistance, hyperinsulinemia; human glucagon-like-peptide-1 mimics and
       their antidiabetic effects)
L34 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:157498 CAPLUS <<LOGINID::20070124>>
DOCUMENT NUMBER: 140:199313
                        Preparation of fused pyrrolylcarboxamides as glycogen
phosphorylase inhibitors
INVENTOR(S): Daisy, Joe
PATENT ASSIGNEE(S): Prizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 71 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:
    PATENT NO.
                               KIND DATE
                                                       APPLICATION NO.
      P 1391460 A1 20040225 EP 2003-20676 20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
    EP 1391460
          IE. FL CY
                              A2 20010404 EP 2000-308131
    EP 1088824
                             A3 20010627
                             B1 20040107
      P 1088624 B1 20040107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, E, SI, LT, LV, FI, RO
(S 2002183369 A1 20021205 US 2002-117370 20020405 <--
    US 2002183369
    US 6576653 B2 20030610
US 2003195361 A1 20031016 US 2003-367002
                                                                                     20030214 <--
US 6828343 B2 20041207
PRIORITY APPLN. INFO.:
                                                       US 1999-157148P
                                   EP 2000-308131 A3 20000918
US 2000-670759 A3 20000927
                                    US 2002-117370
                                                               A3 20020405
OTHER SOURCE(S): MARPAT 140:199313
AN 2004:157498 CAPLUS << LOGINID::20070124>>
ED Entered STN: 26 Feb 2004
TI Preparation of fused pyrrolylcarboxamides as glycogen phosphorylase
```

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

AB Title compds. [I; Q = substituted aryl, heteroaryl; Z, X = C, CH, CH2, N, B 1tite compds. [L Q = substituted anyl, heteroaryl; Z, X = C, CH, CHZ, N, O, S; X1 = NRa, CH2, O, S; dotted lines = bond, null; both dotted lines are not simultaneously bonds; R1 = H, halo, alkoxy, alkylthio, alkyl, CF3, NH2, alkylamino, dialkylamino, NO2, CN, CO2H, carboxyalkyl, alkenyl, alkynyl; Ra, Rb = H, alkyl; Y = CH(OH), null; R2R3 = atoms to form a 5-6 membered ring containing 0-3 heteroatoms and 0-2 double bonds; R4 = COA; A = NRdRd, NRaCH2CH2ORa, N-heterocyclyl; Rd = H, alkyl, alkoxy, aryl, (substituted) aryl, heteroaryl; Rc = H, CO2Ra, ORa, SRa, NRaRa; n = 1-3], were prepared for treatment of diabetes, insulin resistance, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, cataracts, hyperglycemia, hypercholesterolemia, diabetic reiniopaty, catacates, hyperfylediamia, alpercatolescriberina, hypertrassion, hyperinsidiamia, hyperfylipidemia, alberosclerosis, or tissue ischemia (no data). Thus, 6H-thieno[2,3-b]pyrrole-5-carboxylic acid and (3S)-amino-1-((3R,4S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy4-phenylbutan-1-one were coupled using 4-(dimethylamino)pyridine, 1-hydroxybenzotriazole hydrate and 1-(3-dimethylaminopropyl)-3ethylarbodimide hydrochloride in CH2Clt/DMF to give 6H-thieno[2,3-b]pyrrole-5-carboxylic acid [(15)-benzyl-3-((3R,4S)-dihydroxypyrrolidin-1-

y))-(2R)-hydroxy-3-oxopropy)]amide.

pyrrolylcarboxamide fused prepn glycogen phosphorylase inhibitor; thienopyrrolecarboxamide prepn antidiabetic; diabetes insulin resistance diabetic neuropathy treatment fused pyrrolecarboxamide; diabetic nephropathy retinopathy cataract hyperglycemia hypercholesterolemia hypertension treatment pyrrolecarboxamide; hyperinsulinemia hyperlipidemia atherosclerosis tissue chemia treatment fused pyrrolecarboxamide

IT Ischemia (cardiac, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

IT Antiobesity agents a2-Adrenoceptor antagonists

b-Adrenoceptor agonists
(coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

Sulfonylureas RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

IT Kidney, disease (diabetic nephropathy, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

(diabetic neuropathy, treatment; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

1156-19-0, Tolazamide 2295-31-0D, Thiazolidinedione, derivs. 7440-62-2D, Vanadium, complexes 9004-10-8, Insulin, biological studies 9004-10-8D, Insulin, analogs 10238-21-8, Glibenclarnide 12179-36-1D, Pervanadyl (VO(O2)+), complexes 23602-78-0, Benfluorex 28299-33-4D, Imidazoline, derivs. 29094-61-9, Glipizide 37353-31-4, Vanadate 51037-30-0, Acipimos 51110-01-1D, Sornatostatin, analogs 54870-28-9, Meglitinide 56180-94-0, Acarbose 66529-17-7, Midaglizole 72432-03-2, Miglitol 74772-77-3, Ciglitazone 75358-37-1, Linogliride 79944-58-4, Idazoxan 80879-63-6, Emigliates 43840-29-9, Voglibose 86615-96-5, BRL35135 88431-47-4, Clomoxir 89197-32-0, Efaroxan 90505-66-1, Ro 16-8714 90730-96-4, BRL37344 93479-97-1, Glimepiride 97322-87-7, Troglitazone 104343-33-1, MDIL-25637 105182-54-4, Fluparoxan 105816-04-4, Nateglinide 106612-94-6, Human GLP-1 (-7-37) 107444-51-9, Rat GLP-1(7-36) amide 109229-58-5, Englitazone 10505-64-6, Isaglidole 111025-46-8, Pioglitazone 115656-32-1, D 7114 122320-73-4, Rosiglitazone 122575-28-4, Naglivan 122830-14-2, Deriglidole 124083-20-1, Etomoxir 127214-23-7, Camiglibose 13714-47-5, WAG 994 133107-64-9, Insulin lispro 135062-02-1, Repaglinide 138908-40-4, CL 316243 141200-24-0, Darglitazone 141758-74-9, AC299-1 87887-46-3, Symlin 395214-16-1 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) 1156-19-0, Tolazamide 2295-31-0D, Thiazolidinedione, derivs. 141736-14-9, AC2993 16168-140-3, Symin 395214-15-1 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors) 9001-42-7, a-Glucosidase 9025-82-5, Phosphodiesterase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors) 9035-74-9, Glycogen phosphorylase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; preparation of fused pyrrolylcarboxamides as glycogen

hosphorylase inhibitors) TT 332098-11-0P 332098-12-1P 332098-13-2P 332098-14-3P 332098-15-4P 332098-16-5P 332098-17-6P 332098-18-7P 332098-19-8P 332098-20-1P 332098-22-3P 332098-23-4P 332098-29-0P 332098-20-6P 332098-26-7P 332098-27-8P 332098-28-9P 332098-29-0P 332098-30-3P 332098-31-4P 332098-32-5P 332098-33-6P 332098-34-7P 332098-35-8P 332098-36-9P 332098-37-0P 332098-38-1P 332098-39-2P 332098-40-5P 332098-41-6P 332098-42-7P 332098-43-8P 332098-44-9P 332098-45-0P 332098-46-IP 332098-47-2P 332098-48-3P 332098-49-4P 332098-50-7P 332098-52-9P 332098-54-IP 332098-55-2P 332098-57-4P 332098-59-6P 332098-61-0P 332098-63-2P 332098-65-4P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

IT Eve. disease

eye, cuscase (diabetic retinopathy, treatment; preparation of fused pyrrolylcarboxamide: as glycogen phosphorylase inhibitors)

(fatty acid oxidation inhibitors coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

Gluconeogenesis

(inhibitors coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibi

Heart, disease

(ischemia, treatment; preparation of fused pyrrolylearboxamides as glycogen phosphorylase inhibitors)

Anti-ischemic agents

Anticholesteremic agents

Antidiabetic agents

Antihypertensives

Drug delivery systems

Human

Hypolipemic agents

(preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

IT Atherosclerosis

Cataract Diabetes mellitus

Hypercholesterole

Hyperglycemia

Hypertension

Hypertriglyceridemia Ischemia

(treatment; preparation of fused pyrrolylcarboxamides as glycogen

phosphorylase inhibitors)

RL: BSU (Biological study, unclassified); BIOL (Biological study) (treatment; preparation of fused pyrrol) carboxamides as glycogen phosphorylase inhibitors)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (g, PPAR-g agonists coadministration; preparation of fused

pyrrolylearboxamides as glycogen phosphorylase inhibitors)
9007-92-5, Glucagon, biological studies 106602-62-4, Amylin
RL: BSU (Biological study, unclassified): BIOL (Biological study)
(antagonists coadministration; preparation of fused pyrrolylearbor

glycogen phosphorylase inhibitors)

IT 56-03-1D, Biguanide, derivs. 64-77-7, Tolbutamide 94-20-2, Chloropropamide 114-86-3, Phenformin 458-24-2, Fenfluramine 657-24-9, Metformin 692-13-7, Buformin 968-81-0, Acetohexamide

IT 637-81-0, Azidoacetic acid ethyl ester 1066-54-2, (Trimethylsilyl)acetylene 1126-09-6, Piperidine-4-carboxylic acid ethyl ester 4530-18-1, Boc-DL-Phenylalanine 6030-36-0, 4-Methylthiophene-2-carboxaldehyde 7283-96-7, 5-Chlorothiophene-2-carboxaldehyde 13679-70-4, 5-Methyl-2-thiophenecarboxaldehyde 13734-34-4, Boc-L-Phenylalanine 14345-97-2, 2-Chloro-3-methylthiophene (preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

IT 65782-04-9P. 5-Chloro-4-methylthiophene-2-carboxaldehyde 238749-54-7P. 63782-04-97, 3-cnioro-4-menyiunopnene-2-carooxatoenyoe 22879-2-Methyl-4H-hieno(3,2-b)pyrrole-5-carboxylic acid ethyl ester 332098-79-0P 332098-81-4P 332098-83-6P, 2-Bromo-6H-hieno(2,3-b)pyrrole-5-carboxylic acid 332098-85-8P, 2-Methyl-6H-hieno(2,3-b)pyrrole-5-carboxylic acid ethyl ester 332098-87-0P, bjpyrrole-5-carboxylic acid ethyl ester 332098-87-0P,
2-Methyl-6H-thieno[2,3-bjpyrrole-5-carboxylic acid 332098-89-2P
332098-91-6P 332098-93-8P 332098-95-0P 332098-97-2P 332098-99-4P
332099-01-1P, 2-Chloro-6H-thieno[2,3-bjpyrrole-5-carboxylic acid ethyl ester 332099-03-P, 2-Chloro-6H-thieno[2,3-bjpyrrole-5-carboxylic acid 332099-05-5P, 2,4-Dichloro-6H-thieno[2,3-bjpyrrole-5-carboxylic acid ethyl ester 332099-07-7P, 2,4-Dichloro-6H-thieno[2,3-bjpyrrole-5-carboxylic acid did 332099-09-P, 2-Bromo-4H-thieno[3,2-bjpyrrole-5-carboxylic acid 332099-01-4P, 4-Bromo-4H-thieno[3,2-bjpyrrole-5-carboxylic acid 332099-01-3P, 2-Bromo-4H-thieno[3,2-bjpyrrole-5-carboxylic acid did 332099-01-3P, 2-Bromo-4H-thieno[3,2-bjpyrrole-5-carboxylic acid 4D, 2-bjpyrrole-5-carboxylic acid 4D, 2-bpyrrole-5-carboxylic acid 4D, 2-bpyrrole-5-carboxylic acid 4D, 2-bpyrrole-5-carboxylic acid 4D, 2-bpyrrole-5-carboxy acid 332099-19-99; 2-Bromo-4H-thieno[3,2-b]pyrrole-3-carboxylic acid 332099-13-9P, 2-Bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid 332099-14-6P, 2-Methyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-16-8P, 2-Cyano-6H-thieno[2,3-b]pyrrole-5-carboxylic acid 332099-18-0P 332099-20-4P 332099-22-6P, 2-Fluoro-4H-thieno[3,2-b]pyrrole-5-carboxylic acid ethyl ester 332099-24-8P, 2-Fluoro-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-26-0P,

```
ester 332099-36-2P, 3-Bromo-4H-thieno[3,2-b]pyrrole-5-carboxylic acid atylester 332099-40-8P, 2-Chloro-4H-thieno[3,2-b]pyrrole-5-carboxylic acid ethyl ester 332099-40-8P, 2-Chloro-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-44-2P, 3-Methyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid ethyl ester 332099-44-2P, 3-Methyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-48-6P, 2-Cyano-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-48-6P, 2-Cyano-4H-thieno[3,2-b]pyrrole-5-carboxylic acid 332099-50-0P, 3-Bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid ethyl ester 332099-52-2P, 3-Bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid 332099-54-4P 332099-55-6P 332099-56-6P, 2-Chloro-3-methyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid sagonaphyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid ethyl ester 332099-58-6P.
     332099-56-6P, 2-Chloro-3-methyl-4H-thieno(3,2-b]pyrrole-5-carboxylic acid ethyl ester 332099-58-8P, 2-Chloro-3-methyl-4H-thieno(3,2-b]pyrrole-5-carboxylic acid 332099-60-2P 332099-62-4P
       RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
(preparation of fused pyrrolylcarboxamides as glycogen phosphorylase
                        THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
 RECORD
(i) Esteve, L; ES 2081747 A 1996 CAPLUS
(2) Hitzel, V; US 4325963 A 1982 CAPLUS
(3) Pfizer, EP 0846464 A 1998 CAPLUS
 L34 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
                                                          2003:570833 CAPLUS << LOGINID::20070124>>
 ACCESSION NUMBER:
 DOCUMENT NUMBER:
                                                            139:111682
ITILE: Combined use of a GLP-1 compound and a modulator of diabetic late complications INVENTOR(S): Knudsen, Lotte Bjerre; Selmer, Johan PATENT ASSIGNEE(S): Novo Nordisk A/S, Den. SOURCE: PCT Int. Appl., 22 pp. CODEN: PIXXD2
DOCUMENT TYPE:
                                                      Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
                                             KIND DATE
                                                                                    APPLICATION NO.
      PATENT NO.
                                                                                                                                       DATE
```

PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2002351753 A1 20030730 AU 2002-351753 20021220 <-EP 1461070 A2 20040929 EP 2002-787467 20021220
EP 1461070 A2 20040929 EP 2002-787467 20021220
ER: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
JP 2005516968 T 20050609 JP 2003-559533 20021220
US 2003144206 A1 20030731 US 2002-328282 20021223 <-RAI DK 2001-1969 A 20011229
DK 2002-7600 A 20020517 PRAI DK 2001-1969 DK 2002-760 DK 2001-969 A 20020517 DK 2001-969 A 20011229 US 2002-350087P P 20020117 WO 2002-DK888 W 20021220 PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

WO 2003059372 ICM A61K038-00
IPCI A61K0038-00 [ICM,7]
IPCR A61K0038-00 [ICM,7]
IPCR A61K0031-00 [IC,*]; A61K0045-00 [I.A]; A61K0031-138
[I,C*]; A61K0031-135 [I.A]; A61K0031-165 [I.C*];
A61K0031-165 [I.A]; A61K0031-167 [I.C*]; A61K0031-167
[I.A]; A61K0031-401 [I.A]; A61K0031-216 [I.A];
A61K0031-401 [I.A]; A61K0031-401 [I.A]; A61K0031-401
[I,C*]; A61K0031-401 [I.A]; A61K0031-404 [I.C*];
A61K0031-403 [I.A]; A61K0031-4184 [I.A]; A61K0031-407
[I.C*]; A61K0031-407 [I.A]; A61K0031-4184 [I.C*];
A61K0031-4166 [I.A]; A61K0031-4184 [I.A]; A61K0031-4188
[I.A]; A61K0031-407 [I.A]; A61K0031-4196 [I.A];
A61K0031-412 [I.C*]; A61K0031-4172 [I.A]; A61K0031-4196
[I.C*]; A61K0031-52 [I.C*]; A61K0031-55 [I.C*];
A61K0031-55 [I.A]; A61K0038-00 [I.C*]; A61K0038-00
[I.A]; A61K0038-26 [I.C*]; A61K0038-26 [I.A];
A61P0030-00 [I.C*]; A61P0003-10 [I.A]; A61P0009-00
[I.C*]; A61P003-00 [I.C*]; A61P0003-02-00
[I.C*]; A61P0035-00 [I.A]; A61P0005-00 [I.A];
A61P0037-00 [I.C*]; A61P0027-02 [I.A];
A61P0037-00 [I.C*]; A61P0037-02 [I.A];
A61F0031-165 [I.A]; A61K0031-165 [I.C*];
A61K0031-165 [I.A]; A61K0031-167 [I.C**]; A61K0031-165 PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,

```
WO 2003059372 A2 20030724 WO 2002-DK888 20021220 <--
WO 2003059372 A3 20040325

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SS, GS, KS, LT, T, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TI, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, PR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002351753 A1 20030730 AU 2002-351753 20021220 <--
EP 1461070 A2 20040929 EP 2002-787467 20021220

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

IP 2005516968 T 20050609 JP 2003-559533 20021220

US 2003144206 A1 20030731 US 2002-328282 20021229

PRIORITY APPLN. INFO: DK 2002-760 A 20021027
          WO 2003059372
                                                                 A2 20030724 WO 2002-DK888
                                                                                                                                                                            20021220 <--
                                                                                                                    ∠0021220

∠0021223 ←

∠0011229 ←

A 20020517

A 20011229

P 200201
                                                                        DK 2002-760
                                                                       DK 2001-969
                                                                        US 2002-350087P P 20020117
WO 2002-DK888 W 20021220
   AN 2003:570833 CAPLUS << LOGINID::20070124>>
              139:111682
           Entered STN: 25 Jul 2003
Combined use of a GLP-1 compound and a modulator of
   diabetic late complications
IN Knudsen, Lotte Bjerre; Selmer, Johan
PA Novo Nordisk A/S, Den.
         PCT Int. Appl., 22 pp.
CODEN: PIXXD2
  DT Patent
LA English
  IC ICM A61K038-00
CC 1-10 (Pharmacology)
   Section cross-reference(s): 2, 63
FAN.CNT 1
          PATENT NO.
                                                              KIND DATE
                                                                                                               APPLICATION NO.
                                                                                                                                                                                  DATE
                VO 2003059372 A2 20030724 WO 2002-DK888 20021220 <--
O 2003059372 A3 20040325
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
   PI WO 2003059372
          WO 2003059372
                      CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
```

[LA]; A61K0031-21 [LC*]; A61K0031-216 [LA];
A61K0031-35 [LC*]; A61K0031-35 [LA]; A61K0031-401
[LC*]; A61K0031-401 [LA]; A61K0031-403 [LC*];
A61K0031-403 [LA]; A61K0031-404 [LA]; A61K0031-407
[LC*]; A61K0031-407 [LA]; A61K0031-4184 [LC*];
A61K0031-4166 [LA]; A61K0031-4184 [LA]; A61K0031-4188
[LA]; A61K0031-496 [LC*]; A61K0031-4196 [LA];
A61K0031-472 [LC*]; A61K0031-472 [LA]; A61K0031-5375
[LC*]; A61K0031-55 [LA]; A61K0031-55 [LC*];
A61K0031-55 [LA]; A61K0038-06 [LC*]; A61K0038-00
[LA]; A61K0038-26 [LC*]; A61K0038-26 [LA];
A61P0003-00 [LC*]; A61P0003-10 [LA]; A61P0009-00
[LC*]; A61P0009-10 [LA]; A61P0009-12 [LA];
A61P0013-00 [LC*]; A61P0013-12 [LA]; A61P0009-00
[LC*]; A61P0009-10 [LA]; A61P0025-02 [LA];
A61P0013-00 [LC*]; A61P0013-12 [LA]; A61P0043-00
[LC*]; A61P0043-00 [LA]; A61P0025-02 [LA];
A61P0013-00 [LC*]; A61P0013-12 [LA]; A61P0043-00
[LC*]; A61F0031-00 [LA]; A61F0031-15 [LC*];
A61K0031-165 [LA]; A61K0031-167 [LC*]; A61K0031-167
[LC*]; A61K0031-138 [LA]; A61K0031-165 [LC*];
A61K0031-165 [LA]; A61K0031-167 [LC*]; A61K0031-167
[LC*]; A61K0031-10 [LA]; A61K0031-167 [LC*]; A61K0031-101
[LC*]; A61K0031-101 [LA]; A61K0031-164 [LC*];
A61K0031-103 [LA]; A61K0031-104 [LA]; A61K0031-107
[LC*]; A61K0031-107 [LA]; A61K0031-104 [LC*]; A61K0031-107
[LC*]; A61K0031-107 [LA]; A61K0031-104 [LA]; A61K0031-107
[LC*]; A61K0031-107 [LA]; A61K0031-104 [LA]; A61K0031-107
[LC*]; A61K0031-107 [LA]; A61K0031-104 [LA]; A61K0031-107
[LC*]; A61K0031-107 [LA]; A61K0031-107
[LC*]; A61K0031-107 [LA]; A61K0031-108 [LC*]; A61K0031-107
[LC*]; A61K0031-107 [LA]; A61K0031-108 [LA]; A61K0031-107
[LC*]; A61K0031-107 [LA]; A61K0031-108 [LA]; A61K0031-107
[LC*]; A61K0031-100 [LC*]; A61K0031-108 [LA]; A61K0031-107
[LC*]; A61K0031-00 [LC*]; A61K0031-108 [LA]; EP 1461070 A61P0027-00 [LC*]; A61P0027-02 [LA]; A61P0043-00 [LC*]; A61P0043-00 [LA]

JP 2005516968 IPCI A61K0038-00 [ICM,7]; A61K0031-138 [ICS,7]; A61K0031-165 [ICS,7]; A61K0031-167 [ICS,7]; A61K0031-16 [ICS,7];

A61K0031-12 [ICS,7]; A61K0031-404 [ICS,7];

A61K0031-403 [ICS,7]; A61K0031-404 [ICS,7];

A61K0031-407 [ICS,7]; A61K0031-4168 [ICS,7];

A61K0031-4184 [ICS,7]; A61K0031-4188 [ICS,7];

A61K0031-4164 [ICS,7]; A61K0031-4196 [ICS,7];

```
A61K0031-472 [ICS,7]; A61K0031-5377 [ICS,7];
A61K0031-5375 [ICS,7,C*]; A61K0031-55 [ICS,7];
A61K0045-00 [ICS,7]; A61F0003-10 [ICS,7]; A61F0003-00
[ICS,7,C*]; A61F0009-10 [ICS,7]; A61F0009-12 [ICS,7];
A61F0013-00 [ICS,7,C*]; A61F00025-00 [ICS,7];
A61F0013-00 [ICS,7,C*]; A61F00025-00 [ICS,7];
A61F0013-00 [ICS,7,C*]; A61F0027-02 [ICS,7];
A61F0025-02 [ICS,7]; A61F0027-02 [ICS,7]; A61F0027-00
[ICS,7,C*]; A61F0043-00 [ICS,7]
[PCR A61K0031-138 [IA]; A61K0031-138 [I,C*]; A61K0031-165
[IA]; A61K0031-167 [I,C*]; A61K0031-138 [I,C*]; A61K0031-216
[IA]; A61K0031-35 [IA]; A61K0031-21 [I,C*]; A61K0031-216
[IA]; A61K0031-401 [IA]; A61K0031-401 [I,C*]; A61K0031-403
[IA]; A61K0031-401 [IA]; A61K0031-401 [I,C*]; A61K0031-4164
[I,C*]; A61K0031-4166 [IA]; A61K0031-4184 [IA];
A61K0031-4188 [IA]; A61K0031-4196 [IA]; A61K0031-4196
[I,C*]; A61K0031-412 [IA]; A61K0031-4196
[I,C*]; A61K0031-472 [IA]; A61K0031-4196
[I,C*]; A61K0031-472 [IA]; A61K0031-4196
[I,C*]; A61K0031-4166 [IA]; A61K0031-4196
[I,C*]; A61K0031-4166
[IA]; A61K0031-4166
```

```
use); BIOL (Biological study); USES (Uses)
(amino acid sequence; combined use of a GLP-1 compound and a modulator of diabetic late complications)

IT 525-66-6, Propranolol 13523-86-9, Pindolol 26839-75-8, Timolol
      $25-\(\delta\)-6-6-6, Propranolol 13523-86-9, Pindolol 2\(\delta\)-63-75-8, Timolol 29122-68-7, Atenolol 37517-30-9, Acebutolol 42200-33-9, Nadolol 51384-51-1, Metoprolol 62571-86-2, Captopril 75847-73-3, Enalapril 76547-98-3, Lisinopril 81147-92-4, Esmolol 33647-97-6, Spirapril 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 89371-37-9, Imidapril 89750-14-1D, GLP-1, analogs or fragments 98048-97-6, Fosinopril 107133-36-8, Perindopril erbumine 114798-26-4, Losartan 135038-57-2, Alatriopril 136087-85-9, Fidarestat 137862-53-4, Valsartan 138402-11-6, Irbesartan 141732-76-5, Exendin-4, derivs. 16993-94-0, Ly 33531

KL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combined use of a GLP-1 compound and a modulator of diabetic late complications)
        diabetic late complications)
9015-82-1, Angiotensin-converting enzyme 9028-31-3, Aldose reductase
141436-78-4, Protein kinase C
        RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (inhibitors; combined use of a GLP-1 compound and a modulator of diabetic late complications)
134 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2003:320036 CAPLUS <<LOGINID::20070124>>
 DOCUMENT NUMBER:
                                                                            138:338498
                                      Preparation of human glucagon-like-peptide-1 mimics and their use in the treatment of diabetes
and their use in the treatment of diabetes
and related conditions
INVENTOR(S): Natarajan, Sesha I.; Bastos, Margarita M.;
Bernatowicz, Michael S.; Mapelli, Claudio; Lee, Ving;
Ewing, William R.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 153 pp.

CODEN: PIXXD2

COCUMENT TARES
                                                         Patent
English
 DOCUMENT TYPE:
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:
        PATENT NO.
                                                         KIND DATE
                                                                                                         APPLICATION NO.
                                                                                                                                                                         DATE
        WO 2003033671
                                                                                                      WO 2002-US33386
                                                             A2 20030424
        WO 2003033671
                                                              A3 20051229
              W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
```

```
4C206/ZA33; 4C206/ZA36; 4C206/ZA42; 4C206/ZA81;
4C206/ZA33; 4C206/ZA36; 4C206/ZA42; 4C206/ZA42; 4C206/ZA36; 4C206/ZC42

4C206/ZC20; 4C206/ZC35; 4C206/ZC42

US 2003144206 IPC1 A61K0038-26 [ICM,7]; A61K0031-401 [ICS,7]

IPCR A61K0031-401 [LC°]; A61K0031-401 [LA]; A61K0038-26

[LC°]; A61K0038-26 [LA]

NCL 514/012.000; 514/423.000

AB Methods and uses for treatment of diabetic late complications comprising
    administration of a GLP-1 compound and a modulator of
      liabetic complications.
ST GLP1 diabetes late complication therapy; glucagon like peptide I analog fragment antidiabetic
IT Angiotensin receptor antagonists
     Antihypertensives
    Human
      Hypertension
    Protein sequences
    b-Adrenoceptor antagonists
    b1-Adrenoceptor antagonists
(combined use of a GLP-1 compound and a modulator of
          iabetic late complications)
IT Kidney, disease
       (diabetic nephropathy; combined use of a GLP-
         compound and a modulator of diabetic late complications)
     Nerve, disease
(diabetic neuropathy; combined use of a GLP-1
        compound and a modulator of diabetic late complications)
      Eye, disease
       (diabetic retinopathy; combined use of a GLP-1 compound and a modulator of diabetic late complications)
IT Gene animal
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (glp-1; combined use of a GLP-1
ggp-1, compound and a modulator of diabetic late complications)

ID Diabetes mellitus
(non-insulin-dependent; combined use of a GLP-1
compound and a modulator of diabetic late complications)

IT Antidiabetic agents
    Drug delivery systems
(oral; combined use of a GLP-1 compound and a
        modulator of diabetic late complications)
     Drug delivery systems
(parenterals; combined use of a GLP-1 compound and a
         nodulator of diabetic late complications)
    RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
```

```
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FL, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SL, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FL, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2463908
A1 20030424
CA 2002-2463908
20021018 <--
PJ 2005514337
T 20055019 JP 2003-536401
20021018
CN 1630709
A 20050622
CN 2002-820558
20021018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SL, LT, LV, FL, RO, MK, CY, AL, TR, BG, CZ, EE, SK
BR 2002013377
A 20060523
BR 2002-133377
DN 2004001203
A 2004061010
NO 2004-1203
ZA 2004002846
A 20050816
ZA 2004-2846
DTHER SOURCE(S):
MARPAT 138:3338498

***CONTINE CAPITAL STANDARD CAPITAL SCANDARD CAPITAL SCANDAR
    OTHER SOURCE(S): MARPAT 138:338498
AN 2003:320036 CAPLUS <<LOGINID::20070124>>
DN 138:338498
     ED Entered STN: 25 Apr 2003
    TI Preparation of human glucagon-like-peptide-1 mimics and their use in the treatment of diabetes and related conditions
    IN Natarajan, Sesha I.; Bastos, Margarita M.; Bernatowicz, Michael S.;
Mapelli, Claudio; Lee, Ving; Ewing, William R.
PA Bristol-Myers Squibb Company, USA
    SO PCT Int. Appl., 153 pp.
CODEN: PIXXD2
 LA English
                    ICM C12N
    CC 34-3 (Amino Acids, Peptides, and Proteins)
    Section cross-reference(s): 1, 63
FAN.CNT 2
PATENT NO. KIND DA
                                                                                                                                                                         APPLICATION NO.
                                                                                                  KIND DATE
  PI WO 2003033671
                                                                                                           A2 20030424 WO 2002-US33386
                                                                                                                                                                                                                                                                                            20021018 <--
                 WO 2003033671 AZ 20031229
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
                                     PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
```

```
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NR, SN, TD, TG CA 2463908 A1 20030424 CA 2002-2463908 20021018 <- Description of the control of th
PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

WO 2003033671 ICM C12N

IPCI C12N [ICM,7]

IPCR A61K0038-00 [LC*]; A61K0038-00 [LA]; A61K0038-26

[LC*]; A61K0038-26 [LA]; A61P0003-06 [LA]; A61P0003-10

[LA]; A61P0003-00 [LC*]; A61P0003-06 [LA]; A61P0003-10

[LA]; A61P0003-00 [LC*]; A61P0003-10 [LA]; A61P0009-12

[LA]; A61P0013-00 [LC*]; A61P0017-02 [LA]; A61P0029-12

[LA]; A61P0017-00 [LC*]; A61P0017-02 [LA]; A61P0025-00

[LC*]; A61P0027-00 [LA]; A61P0017-02 [LA]; A61P003-00

[LA]; C07K007-00 [LA]; A61P0037-00 [LC*]; A61P003-00

[LA]; C07K007-00 [LA]; C07K0014-00 [LC*]; C07K0014-00

[LA]; C07K0014-435 [LC*]; C07K0014-635 [LA];

ECLA C07K014-435 [LC*]; C07K0014-435 [ICM,7,C*];

C07K007-06 [ICS,7]; C07K0010-435 [ICS,7];

PCR A61K0038-08 [ICS,7]; A61K0038-26 [LA]; A61F0003-00

[LC*]; A61K0038-06 [LC*]; A61F0003-00 [LA]; A61F0003-10

[LA]; A61P0003-00 [LC*]; A61P0003-00 [LA*]; A61P0003-10

[LA]; A61P0003-00 [LC*]; A61P0003-50 [LA];

A61P0003-00 [LC*]; A61P001-12 [LA];

A61P0017-00 [LC*]; A61P001-12 [LA];

A61P0017-00 [LC*]; A61P001-12 [LA];

A61P0027-02 [LA]; A61P0043-00 [LC*]; A61P0043-00
                                                                                                                                                                                                       CLASS PATENT FAMILY CLASSIFICATION CODES
              PATENT NO.
```

```
[I,C*]; A61P0017-02 [I,A]; A61P0025-00 [I,C*];
A61P0025-00 [I,A]; A61P0027-00 [I,C*]; A61P0027-02
[I,A]; A61P0043-00 [I,C*]; A61P0043-00 [I,A];
C07K0002-00 [I,C]; C07K0002-00 [I,A]; C07K0007-00
                                                               [LC*]; C07K0007-06 [LA]; C07K0007-08 [LA];
C07K0014-00 [LC*]; C07K0014-00 [LA]; C07K0014-435
  [I,C*]; C07K0014-605 [I,A]

ECLA C07K014/605

BR 2002013377 IPCI A61K0038-00 [ICS,7]; A61K0038-08 [ICS,7]; C07K0002-00
                                              [ICS,7]
IPCR A61K0038-00 [N,C*]; C07K0014-435 [L,C*]; A61K0038-00
[ICS,7]

IPCR A61K0038-00 [N,C*]; C07K0014-435 [I,C*]; A61K0038-00
[N,A]; C07K0014-605 [I,A]

ECLA C07K014/605

NO 2004001203 IPCI C07K0014-605 [ICM,7]; C07K0014-435 [ICM,7,C*];
C07K0004-00 [ICS,7]; A61K0038-26 [ICS,7]; A61K0038-08
[ICS,7]; A61K0038-00 [I,C*]; A61K0038-00 [I,A]; A61K0038-26
[I,C*]; A61K0038-26 [I,A]; A61P0003-00 [I,C*];
A61P0003-04 [I,A]; A61P0003-00 [I,A]; A61P0003-10
[I,A]; A61P0003-00 [I,C*]; A61P0003-50 [I,A];
A61P0003-00 [I,C*]; A61P0003-10 [I,A]; A61P0009-12
[I,A]; A61P0013-00 [I,C*]; A61P0013-12 [I,A]; A61P0009-12
[I,A]; A61P0027-00 [I,C*]; A61P0013-10 [I,C*]; A61P003-00 [I,C*]; A61P0013-10 [I,C*]; A61P003-00 [I,C*]; C07K007-06 [I,A];
C07K0007-08 [I,A]; C07K0014-00 [I,C*]; C07K0014-00
[I,A]; C07K0014-435 [I,C*]; C07K0014-605 [I,A];
ECLA C07K014/605

ZA 2004002846 IPCR A61K0038-00 [N,C*]; C07K0014-35 [I,C*]; A61K00
   ZA 2004002846 IPCR A61K0038-00 [N,C*]; C07K0014-435 [L,C*]; A61K0038-00 [N,A]; C07K0014-605 [LA] ECLA C07K014/605
     OS MARPAT 138:338498
 OS MARPAT 138:338498

AB The invention provides novel human glucagon-like peptide-1 (GLP-
1) peptide mimics A-Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Xaa6-Xaa7-Xaa8-Xaa9-Y-
Z-B [Xaa1-Xaa9 are naturally or non-naturally occurring armino acid residues; Y and Z are amino acid residues which may be substituted; A and B are optionally present; A is H, an amino acid or peptide containing .apprx. 
1-15 amino acid residues, an R group [H, (cyclo)alkyl, cycloxalkylalkyl, heterocyclyl, heterocycloalkyl, (heteroparylarylarylalkyl, aryloxyalkyl, heteroarylalkyl, or heteroaryloxyalkyl, and RCO (amide) group, a carbamate group, a urea, a sulfonarmido, or an aminosulfonyl group; B is OH, alkoxy, ctc., an amino or amino acid residue, or a neotide containing from 1-15 amino
              etc., an amino or amino acid residue, or a peptide containing from 1-15 amino acid residues, terminating at the C-terminus as a carboxamide, ester, carboxyl, or an amino alc.] that mimic the biol. activity of the native
```

GLP-I peptide and thus are useful for the treatment or

```
[LA]; C07K0007-00 [LC*]; C07K0007-06 [LA];
C07K0007-08 [LA]; C07K0014-00 [LC*]; C07K0014-00
[LA]; C07K0014-435 [LC*]; C07K0014-605 [LA];
S14337 IPC1 C07K0007-06 [ICM,7]; A61K0038-00 [ICS,7]; A61P0003-04
[ICS,7]; A61P0003-06 [ICS,7]; A61P0005-50 [ICS,7];
A61P0003-00 [ICS,7,C*]; A61P0009-10 [ICS,7];
A61P0005-00 [ICS,7]; A61P0009-10 [ICS,7];
A61P0013-12 [ICS,7]; A61P0013-00 [ICS,7,C*];
A61P0013-12 [ICS,7]; A61P0013-00 [ICS,7,C*];
A61P0017-02 [ICS,7]; A61P0017-00 [ICS,7,C*];
A61P0025-00 [ICS,7]; A61P0017-00 [ICS,7];
C07K0007-00 [ICS,7]; A61P0017-00 [ICS,7];
A61P0025-00 [ICS,7]; A61P0017-00 [ICS,7];
A61P0025-00 [ICS,7]; A61P0017-00 [ICS,7];
C07K0007-00 [ICS,7]; C07K0014-00 [ICS,7];
A61K0038-26 [ICS,7]

IPCR A61K0038-00 [N,A]; A61K0038-00 [N,C*]; C07K0014-435
[LC*]; C07K0014-605 [LA]

FTERM 4C084/AA02; 4C084/AA06; 4C084/AA07; 4C084/BA01;
4C084/BA08; 4C084/BA17; 4C084/BA23; 4C084/BA32; 4C084/CA59; 4C
                                                                                                                                [LA]; C07K0007-00 [LC*]; C07K0007-06 [LA];
  JP 2005514337
                                                                              CN 1630709
EP 1572892
```

```
prevention of diseases or disorders associated with GLP activity. These chemical-modified peptides stimulate insulin secretion in type II diabetics and produce other beneficial insulinotropic responses, while exhibiting increased stability to proteolytic cleavage making them ideal therapeutic candidates for oral or parenteral administration. A method of preparing the polypeptides comprises replacing the message sequence of the polypeptide with a variant message sequence capable of inducing receptor mediated signal transduction. An example is claimed peptide H-AEGTFTSD-Bip(2-Et)-Bip(2-Me)-NH2 (Bip = biphenylalanine residue).

ST glucagon like peptide mimic prepn treatment diabetes
IT Antiarteriosclerotics (antiatherosclerotics; preparation of human glucagon-like-peptide-1 mimics
             (antiatherosclerotics; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)
  IT Kidney, disease
             (diabetic nephropathy; preparation of human glucagon-like-peptide-
l mimics for use in treatment of diabetes and related
               conditions)
 IT Nerve, disease
             (diabetic neuropathy; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)
          Eye, disease
             (diabetic retinopathy; preparation of human glucagon-like-peptide-1 mimics
          for use in treatment of diabetes and related conditions)
Metabolic disorders
             (metabolic syndrome X; preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)
  IT Antidiabetic agents
         Antihypertensives
         Antiobesity agents
        Atherosclerosis
Diabetes mellitus
         Hyperglycemia
           Hypertension
         Hypertriglyceridemia
        Hypolipemic agents
Obesity
         Obesity
Wound healing
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of
diabetes and related conditions)
```

IT Hyperlipidemia
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions) IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

```
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)

IT 89750-14-1DP, Glucagon-like peptide I, mimics 516514-32-2P
516514-38-8P 516514-43-5P 516514-47-9P 516514-52-6P 516514-55-9P
516514-38-8P 516514-43-5P 516514-47-9P 516514-52-6P 516514-72-0P
516514-75-3P 516514-78-6P 516514-47-9P 516514-68-4P 516514-72-0P
516514-75-3P 516514-78-6P 516514-81-PP 516514-68-4P 516514-78-0P
516515-09-6P 516515-14-3P 516515-18-7P 516515-03-0P 516515-06-3P
516515-30-3P 516515-34-7P 516515-38-1P 516515-22-3P 516515-26-7P
516515-30-3P 516515-34-7P 516515-38-1P 516515-22-3P 516515-68-7P 516515-59-7P 516515-59-7P 516515-59-7P 516515-59-7P 516515-59-7P 516515-59-7P 516515-69-7P 516516-60-1P 516516-60-2P 516516-68-0P 516516-68-0P 516516-60-2P 516516-60-2P 516516-68-0P 516516-68-0P 516516-69-59 516516-69-59 516517-02-5P 516517-03-9P 516517-03-P 516516-70-0P 516516-70-0P 516516-69-59 516517-02-5P 516517-03-9P 516517-03-P 516517-03-P 516517-03-P 516517-03-P 516517-03-P 516517-03-P 516517-33-2P 516517-33-P 516518-33-5P 516518-30-0P 516518-30-3P 516518-30-3P 516518-30-3P 516518-30-3P 516518-30-3P 516518-30-3P 516518-30-3P 516519-30-3P 516519-30-3
     L34 ANSWER 5 OF 9 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
      ACCESSION NUMBER: 2003:390202 BIOSIS << LOGINID::20070124>> DOCUMENT NUMBER: PREV200300390202
                                                                  The glucagon-like peptides: A double-edged therapeutic
       TITLE:
      AUTHOR(S): Perry, TracyAnn [Reprint Author]; Greig, Nigel H.
CORPORATE SOURCE: Section of Drug Design and Development, Laboratory of
Neurosciences, Gerontology Research Center, National
                                                      Institute on Aging, National Institutes of Health, 5600
Nathan Shock Drive, Baltimore, MD, 21224, USA
     National Stock Drive, Baltimore, MD, 21224, USA pernyl@grc.nia.nib.gov

SOURCE: Trends in Pharmacological Sciences, (July 2003)

Vol. 24, No. 7, pp. 377-383, print.

ISSN: 0165-6147 (ISSN print).

DOCUMENT TYPE: Article
     AN 2003:390202 BIOSIS <<LOGINID::20070124>>
DN PREV2003003090202
TI The glucagon-like peptides: A double-edged therapeutic sword?.
AU Perry, TracyAnn [Reprint Author]; Greig, Nigel H.
CS Section of Drug Design and Development, Laboratory of Neurosciences, Gerontology Research Center, National Institute on Aging, National Institutes of Health, 5600 Nathan Shock Drive, Baltimore, MD, 21224, USA
     perryt@grc.nia.nih.gov
SO Trends in Pharmacological Sciences, (July 2003) Vol. 24, No. 7,
                pp. 377-383. print.
ISSN: 0165-6147 (ISSN print).
      DT Article
                General Review; (Literature Review)
       LA English
      ED Entered STN: 27 Aug 2003
     Last Updated on STN: 27 Aug 2003

AB Glucagon-like peptide-1(7-36)-amide (GLP-1) is an endogenous peptide that is secreted from the gut in response to the presence of food. Recent studies have established that GLP-
                      and its longer-acting analog exendin-4 have multiple
               ration is tonger-acting analog extensions have multiple synergistic effects on glucose-dependent, insulin secretion pathways of the pancreatic beta-cell and on plasticity in neuronal cells. Recent interest has focused on the development of these peptides as a novel therapeutic strategy for non-insulin-dependent (type 2) diabetes mellitus and associated neuropathy. This is with a view to developing lead compounds, based on neurotrophic action, for central and peripheral
```

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (preparation of human glucagon-like-peptide-1 mimics for use in treatment of

```
516521-28-IP 516521-29-2P 516521-30-5P 516521-31-6P 516521-32-7P 516521-33-8P 516521-34-9P 516521-35-0P 516521-36-IP 516521-37-2P 516521-38-3P 516521-39-4P 516521-40-7P 516521-41-8P 516521-42-9P 516521-45-P 516521-45-2P 516521-53-2P 516521-54-3P
       RL: PAC (Pharmacological activity); SPN (Synthetic preparation): THU
       (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
          (preparation of human glucagon-like-peptide-1 mimics for use in treatment of
           diabetes and related conditions)
 IT 150-46-9, Triethyl borate 1973-22-4, 1 Bromo 2 ethylbenzene 4326-36-7 16419-60-6, o Tolylboronic acid 93267-04-0 516521-49-6
      16419-60-6, o Tolylboronic acid 93267-04-0 516521-49-6
RL: RCT (Reactant) reagent)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)
90002-36-1P, 2 Ethylphenylboronic acid 112766-18-4P 516521-46-3P 516521-48-5P 516521-49-5 516521-50-9P 516521-51-0P
        RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
(preparation of human glucagon-like-peptide-1 mimics for use in treatment of
     Giabetes and related conditions)

1 51-64-9, Dexamphetamine 94-20-2, Chloropropamide 122-09-8, Phentermine 637-07-0, Cloffbrate 657-24-9, Metformin 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 21187-98-4, Gliclazide 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 49562-28-9, Fenofibrate 56180-94-0, Acarbose 72432-03-2, Miglitol 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 105816-04-4, Nateglinide 106505-56-0, Siburramine 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 141750-63-2, Nisvastatin 141758-74-9, AC 2993 144288-97-1, TS-962 145599-86-6, Cerivastatin 152755-31-2, LY295427 159183-92-3, L750355 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 196808-45-4 199113-98-9 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677
          diabetes and related conditions)
      199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 258345-41-4, GW-409544 262352-17-0, CP 529414 282526-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0,
      KAD1129 335149-17-2, ARHO39242 335149-23-0, NVPDPP-728A 335149-25-
      CP331648 430433-17-3, Glipyride 444069-80-1, Axokine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
          (preparation of human glucagon-like-peptide-1 mimics for use in treatment of diabetes and related conditions)
      degenerative disorders such as stroke and Alzheimer's disease in addition
      to the peripheral neuropathy associated with type 2 diabetes mellitus. Here, we address recent advances in the biological action of GLP-1 and its related analogs.
CC Cytology - Animal 02506

Biochemistry studies - Proteins, peptides and amino acids 10064

Biochemistry studies - Carbohydrates 10068
      Pathology - Therapy 12512
Metabolism - Metabolic disorders 13020
      Cardiovascular system - Blood vessel pathology 14508
Endocrine - General 17002
     Endocrine - Pancreas 17008
Endocrine - Pancreas 17008
Endocrine - Neuroendocrinology 17020
Nervous system - Physiology and biochemistry 20504
Nervous system - Pathology 20506
Pharmacology - General 22002
 IT Major Concepts
          Endocrine System (Chemical Coordination and Homeostasis): Nervous
       System (Neural Coordination); Pharmacology
Parts, Structures, & Systems of Organisms
         beta cells: endocrine system; neuronal cells: nervous system
          Alzheimer's disease: behavioral and mental disorders, nervous system
          Alzheimer Disease (MeSH)
       Discases
          diabetic neuropathy: endocrine disease/pancreas, metabolic disease,
          nervous system disease
Diabetic Nephropathies (MeSH)
       Diseases
          stroke: nervous system disease, vascular disease
          Cerebrovascular Disorders (MeSH)
          type 2 diabetes mellitus: endocrine disease/pancreas,
           netabolic disease
Diabetes Mellitus, Non-Insulin-Dependent (MeSH)
IT Chemicals & Biochemicals
         glucagon-like peptide-1(7-36)-amide; glucose; insulin
        Miscellaneous Descriptors
drug development
RN 118549-37-4 (glucagon-like peptide-1(7-36)-amide)
      50-99-7Q (glucose)
58367-01-4Q (glucose)
```

9004-10-8 (insulin)

```
L34 ANSWER 6 OF 9 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
       DUPLICATE I
 ACCESSION NUMBER: 2001:506591 BIOSIS <<LOGINID::20070124>> DOCUMENT NUMBER: PREV200100506591
                             Urinary excretion of glucagon-like peptide 1 (GLP
-1) 7-36 amide in human type 2
-1) 7-30 artiude in numan type 2
(non-insulin-dependent) diabetes mellitus.

AUTHOR(S): Lugari, R. [Reprint author]; Ugolotti, D.; Dei Cas, A.;

Barilli, A. L.; lotti, M.; Marani, B.; Orlandini, A.;

Gnudi, A.; Zandomeneghi, R.

CORPORATE SOURCE: Cattedra di Endocrinologia, Via Gramsci 14, 43100, Parma,
htaly
endoparm@ipruniv.cce.unipr.it

SOURCE: Hormone and Metabolic Research, (September, 2001)
Vol. 33, No. 9, pp. 568-571. print.
CODEN: HMMRA2. ISSN: 0018-5043.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Oct 2001
Last Updated on STN: 23 Feb 2002
AN 2001:506591 BIOSIS <<LOGINID::20070124>>
DN PREV200100506591
 TI Urinary excretion of glucagon-like peptide 1 (GLP-1)
7-36 amide in human type 2 (non-insulin-dependent) diabetes
 AU Lugari, R. [Reprint author]; Ugolotti, D.; Dei Cas, A.; Barilli, A. L.;
lotti, M.; Marani, B.; Orlandini, A.; Gnudi, A.; Zandomeneghi, R. CS Cattedra di Endocrinologia, Via Gramsci 14, 43100, Parma, Italy
endoparm@ipr.miv.cce.unipr.it

SO Hormone and Metabolic Research, (September, 2001) Vol. 33, No. 9, pp. 568-571, print.

CODEN: HMMRA2. ISSN: 0018-5043.
DT Article
LA English
 ED Entered STN: 31 Oct 2001
ED Entered STN: 31 Oct 2001

Last Updated on STN: 23 Feb 2002

AB The urinary excretion of insulinotropic glucagon-like peptide 1 (
GLP-1) was investigated as an indicator of renal tubular integrity in 10 healthy subjects and in 3 groups of type 2 diabetic patients with different degrees of urinary albumin excretion rate. No significant difference emerged between the groups with respect to age of the patients, known duration of diabetes, metabolic control,

DMI existing that have a subject to the property of the patients.
       BMI, or residual beta-cell pancreatic function. Endogenous creatinine clearance was significantly reduced under conditions of overt diabetic
        nephropathy, compared with normo and microalbuminuric patients
```

```
RN 60-27-5 (creatinine)
ANSWER 7 OF 9 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights
 reserved on STN
ACCESSION NUMBER: 96034762 EMBASE <<LOGINID::20070124>>
ACCESSION NUMBER: 96034762 EMBASE <LOGINID::20070124:
DOCUMENT NUMBER: 1996034762

TITLE: Gastric emptying, glucose responses, and insulin secretion after a liquid test meal: Effects of exogenous glucagon-like peptide-1 (GLP-1)-(7-36) amide in type 2 (noninsulin-dependent) diabetic patients.

AUTHOR: Willms B.; Werner J.; Holst J.J.; Orskov C.; Creutzfeldt W.; Nauck M.A.

CORPORATE SOURCE.
 CORPORATE SOURCE: Department of Medicine, Ruhr-University Bochum,
Knappschafts-Krankenhaus, In der Schornau 23-25,44892
                        Radpisciator-Kraterinats, in the Scholiau 63/23,4492
Bochum, Germany
Journal of Clinical Endocrinology and Metabolism, (
1996) Vol. 81, No. 1, pp. 327-332.
ISSN: 0021-972X CODEN: JCEMAZ
COUNTRY: United States
DOCUMENT TYPE: Journal, Article
FILE SEGMENT: 003 Endocrinology
037 Drug Literature Index
LANGUAGE: English
 LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 1996
Last Updated on STN: 20 Feb 1996
AN 96034762 EMBASE <<LOGINID::20070124>>
 DN 1996034762
 TI Gastric emptying, glucose responses, and insulin secretion after a liquid test meal: Effects of exogenous glucagon-like peptide-1 (GLP-1)-(7-36) amide in type 2 (noninsulin-dependent) diabetic
 patients.

AU Willms B.; Werner J.; Holst J.J.; Orskov C.; Creutzfeldt W.; Nauck M.A.

CS Department of Medicine, Ruhr-University Bochum, Knappschafts-Krankenhaus,
      In der Schornau 23-25.44892 Bochum, German
 81, No. 1, pp. 327-33492 Cochurt, Germany
81, No. 1, pp. 327-332.
ISSN: 0021-972X CODEN: JCEMAZ
  CY United States
 DT Journal; Article
FS 003 Endocrinology
                Drug Literature Index
      037
  LA English
 SL English
ED Entered STN: 20 Feb 1996
      Last Undated on STN: 20 Feb 1996
 AB The aim of the study was to investigate whether inhibition of gastric
```

```
(p<0.01). Urinary excretion of GLP-1 was
      (p<u,vi). Unnary excretion of cult-1 was significantly higher in normoalbuminuric patients compared to controls (490.4+-211.5 vs. 275.5+-132.1 pg/min; p<0.05), with further increase under incipient diabetic nephropathy conditions (648.6+-305) pg/min; p<0.01). No significant difference resulted, in contrast, between
      macroproteinuric patients and non-diabetic subjects. Taking all patients examined into account, a significant positive relationship emerged between
      urinary GLP-1 and creatinine clearance (p=0.004). In conclusion, an early tubular impairment in type 2 diabetes would occur before the onset of glomerular permeability alterations. The tubular dysfunction seems to evolve with the development of persistent
      microalbuminuria. Finally, the advanced tubular involvement, in terms of
      urinary GLP1 excretion, under overt diabetic nephropathy
conditions would be masked by severe concomitant glomerular damage with
       the coexistence of both alterations resulting in a peptide excretion
      similar to control subjects.
CC Biochemistry studies - Proteins, peptides and amino acids 10064
Metabolism - Metabolic disorders 13020
Urinary system - Pathology 15506
Endocrine - General 17002
      Endocrine - Pancreas 17008
       Major Concepts
Clinical Endocrinology (Human Medicine, Medical Sciences); Nephrology
          (Human Medicine, Medical Sciences)
         diabetic nephropathy: endocrine disease/pancreas, metabolic disease, urologic disease
         Diabetic Nephropathies (MeSH)
         type 2 diabetes mellitus: endocrine disease/pancreas,
          metabolic disease, non-insulin-dependent diabetes mellitus
Diabetes Mellitus, Non-Insulin-Dependent (MeSH)
Diabetes Mellitus, Non-Insulin-Dependent (MeSH)
IT Chemicals & Biochemicals
creatinine; glucagon-like peptide 1: renal tubular integrity indicator;
glucagon-like peptide 1 7-36 amide [GLP-1 7-36
amide]: urinary excretion
IT Miscellaneous Descriptors
glomerular permeability
ORGN Classifier
         Hominidae 86215
      Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
      Organism Name
```

. Animals, Chordates, Humans, Mammals, Primates, Vertebrates

emptying of meals plays a role in the mechanism of the blood glucose-lowering action of glucagon-like peptide-1-(7-36) amide [GLP-1-(7-36) amide] in type 2 diabetes. Eight poorly controlled type 2 diabete patients (age, 58 ± 6 yr; body mass index, 30.0 ± 5.2 kg/m2; hemoglobin A(1c), 10.5 ± 1.2%) were studied in the fasting state (plasma glucose, 11.1 ± 1.1 mmol/L). A liquid meal of 400 mL containing 8% arnino acids and 50 g sucrose (327 Kcal) was administered at time zero by a nasogastric tube. Gastric volume was determined by a dye dilution technique using phenol red. In randomized order, GLP-1-(7-36) amide (1.2 pmol/kg·min; Saxon Biochemicals) or placebo (0.9% NaCl with 1% human serum albumin) was infused between -30 and 240 min. In the control experiment, gastric emptying was completed within 120 min, and plasma glucose, insulin, C-peptide, GLP-1-(7-36) amide, and glucagon concentrations transiently increased. With exogenous GLP-1-(7-36) amide (plasma level, apprx.70 pmol/L), gastric volume remained constant over the period it was measured (120 min; P < 0.0001 vs. placebo), and plasma glucose fell to normal fasting values (5.4 ± 0.7 mmol/L) within 3-4 h, whereas insulin was stimulated in most, but not all, patients, and glucagon remained at the basal level or was slightly suppressed. In conclusion, GLP-1-(7-36) amide inhibits gastric emptying in type 2 diabetic patients. Together with the stimulation of insulin and the inhibition of glucagon secretion, this effect probably contributes to the blood glucose-lowering action of GLP-1-(7-36) amide in type 2 diabetic patients when studied after meal ingestion. At the degree observed, inhibition of gastric emptying, however, must be overcome by tachyphylaxis, reduction in dose, or pharmacological interventions so as not to interfere with the therapeutic use of GLP-1-(7-36) amide in type 2 diabetic patients.

CT Medical Descriptors:

insulin release
*non insulin dependent diabetes mellitus: TH, therapy

*non insulin dependent diabetes mellitus
*stomach emptying
adult
aged
article
clinical article
clinical article
clinical article
diabetic angiopathy: CO, complication
diabetic neuropathy: CO, complication
diabetic neuropathy: CO, complication
diabetic neuropathy: CO, complication
diabetic retinopathy

```
drug effect
      drug mechanism
female
      glucagon release
       glucose blood level
       hormone inhibition
         hypertension: DT, drug therapy
      intravenous drug administra
      male
      postprandial state
      priority journal 
randomized controlled trial
      Drug Descriptors:
       Brug Descripturs

*glucagon like peptide 1 [7-36] amide: CM, drug comparison

*glucagon like peptide 1 [7-36] amide: DT, drug therapy

*glucagon like peptide 1 [7-36] amide: PD, pharmacology
       *glucagon like peptide 1 [7-36] amide: CT, clinical trial
*glucose: EC, endogenous compound
*insulin: EC, endogenous compound
      acarbose: DT, drug therapy
captopril plus hydrochlorothiazide: DT, drug therapy
      glibenclamide: DT, drug therapy
isosorbide dinitrate: DT, drug therapy
      metformin: DT, drug therapy
       metoprolol: DT, drug therapy
metoprolol: DT, drug therapy nifedipine: DT, drug therapy placebo: CM, drug comparison RN (glucagon like peptide 1 [7-36] amide) 119637-73-9; (glucose) 50-99-7, 84778-64-3; (insulin) 9004-10-8; (acarbose) 56180-94-0; (glibenclamide) 10238-21-8; (isosorbide dinitrate) 87-33-2; (metformin) 1115-70-4, 657-24-9; (metoprolol) 37350-58-6; (nifedipine) 21829-25-4 CO Saxon (Germany)
 L34 ANSWER 8 OF 9 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights
      reserved on STN
                                                                       DUPLICATE 2
 ACCESSION NUMBER: 93286381 EMBASE <<LOGINID::20070124>> DOCUMENT NUMBER: 1993286381
                            Preserved incretin effect in type 1 diabetic patients with
                      end-stage nephropathy treated by combined
heterotopic pancreas and kidney transplantation.
Nauck M.A.; Busing M.; Orskov C.; Siegel E.G.; Talartschik
 AUTHOR:
                    J.; Baartz A.; Baartz T.; Hopt U.T.; Becker H.-D.;
Creutzteidt w.

CORPORATE SOURCE: Div. of Gastroenterol./Endocrinology, Department of
Medicine, Georg August University, Robert-Koch-Strasse
```

(incretin effect). Insulin responses after the oral glucose challenge (incretin effect). Insulin responses after the oral glucose challenge were similar in the two patient groups despite systemic venous drainage of the pancreas graft in the pancreas-kidney-transplanted group. In both groups GIP and GLP-1 increased after oral but not after intravenous glucose, and B cell secretory responses were significantly smaller (by 55.2 ± 7.7% and 46.5 ± 12.5%, respectively) with 'isoglycaemic' intravenous glucose infusions. The lack of reduction in the incretin effect in pancreas-kidney-transplanted patients, whose functioning pancreas is denervated, indicates a lesser role for the nervous system and a more important contribution of circulating incretin hormones in mediating the enteroinsular axis in man. CT Medical Descriptors:

*diabetic nephropathy: SU, surgery

*insulin dependent diabetes mellitus

*kidney transplantation pancreas transplantation article clinical article controlled study human Drug Descriptors: gastric inhibitory polypeptide: EC, endogenous compound glucagon like peptide 1: EC, endogenous compound *insulin: EC, endogenous compound RN (gastric inhibitory polypeptide) 59392-49-3; (glucagon like peptide 1) 89750-14-1; (glucose) 50-99-7, 84778-64-3; (insulin) 9004-10-8 L34 ANSWER 9 OF 9 MEDLINE on STN
ACCESSION NUMBER: 92288534 MEDLINE <<LOGINID::20070124>>
DOCUMENT NUMBER: PubMed ID: 1600330
TITLE: Basal and nutriem-stimulated pancreatic and gastrointestinal hormone concentrations in type-1-diabetic patients after successful combined pancreas and kidney transplantation Nauck M A; Busing M; Orskov C; Siegel E G; Talartschik J; AU HOR: Nauck M A; Busing M; Orsko C; Stegel E C; Tatartschik
Baartz A; Baartz T; Holzer H; Hopt U T; Ebert R; +
CORPORATE SOURCE: Abteilung Gastroenterologie und Endokrinologie,
Georg-August-Universitat, Gottingen.

SOURCE: The Clinical investigator, (1992 Jan) Vol. 70,
No. 1, pp. 40-8.
Journal code: 9207154, ISSN: 0941-0198. PUB. COUNTRY: GERMANY: Germany, Federal Republic of

```
40,W-3400 Gottingen, Germany
Acta Diabetologica, (1993) Vol. 30, No. 1, pp.
39-45. .
 SOURCE:
                        ISSN: 0940-5429 CODEN: ACDAEZ
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
                      006 Internal Medicine
029 Clinical Biochemistry
 LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Oct 1993
                       Last Updated on STN: 31 Oct 1993
 AN 93286381 EMBASE <<LOGINID::20070124>>
 TI Preserved incretin effect in type 1 diabetic patients with end-stage nephropathy treated by combined heterotopic pancreas and kidney
 AU Nauck M.A.; Busing M.; Orskov C.; Siegel E.G.; Talartschik J.; Baartz A.;
Baartz T.; Hopt U.T.; Becker H.-D.; Creutzfeldt W.
CS Div. of Gastroenterol/Endocrinology, Department of Medicine, Georg August University, Robert-Koch-Strasse 40,W-3400 Gottingen, Germany SO Acta Diabetologica, (1993) Vol. 30, No. 1, pp. 39-45.
 CY Germany
DT Journal; Article
FS 003 Endocrinology
006 Internal Medicine
029 Clinical Biochemistry
 LA English
 ED Entered STN: 31 Oct 1993
      Last Updated on STN: 31 Oct 1993
 AB Insulin secretion is stimulated better by oral than by intravenous glucose
     incretin effect). The contribution of the autonomic nervous system to the incretin effect after oral glucose in humans is unclear. We therefore examined nine type I diabetic (insulin-dependent) patients with end-stage nephropathy, studied after combined heterotopic pancreas and
     kidney transplantation, and 7 non-diabetic kidney recipients (matched for creatinine clearance and immunosuppressive medication). The release of gastric inhibitory polyopetide (GIP) and glucagon-like peptide 1 (GLP-1) immunoreactivity and B cell secretory responses
      (IR insulin and C-peptide) to oral (50 g) and 'isoglycaemic' intravenous glucose (identical glycaemic profile)were measured by radioimmunoassay.
      The difference in B cell responses between the two tests represents the contribution of the enteroinsular axis to the response after oral glucose
```

```
LANGUAGE:
                                                      English
  FILE SEGMENT:
                                                       Priority Journals
  ENTRY MONTH:
                                                             199207
 ENTRY DATE: Entered STN: 24 Jul 1992
Last Updated on STN: 24 Jul 1992
Entered Medline: 13 Jul 1992
AN 92288534 MEDLINE <<LOGINID::20070124>>
DN PubMed ID: 1600330
  TI Basal and nutrient-stir
                                                                             lated pancreatic and gastrointestinal hormone
11 Dasas and mutent-sumulated pancreance and gastrointestmal hormone concentrations in type-1-diabetic patients after successful combined pancreas and kidney transplantation.

AU Nauck M A; Busing M; Orskov C; Siegel E G; Talartschik J; Baartz A; Baartz T; Holzer H; Hopt U T; Ebert R; +

CS Abteilung Gastroenterologie und Endokrinologie, Georg-August-Universitat,
Gottingen.

SO The Clinical investigator, (1992 Jan) Vol. 70, No. 1, pp. 40-8.
SO The Climical investigator, (1992 Jan) vol. Journal code: 9207154. ISSN: 0941-0198.

CY GERMANY: Germany, Federal Republic of DT Journal; Article; (JOURNAL ARTICLE)

A English
FS Priority Journals

EM 199207

Descript
 ED Entered STN: 24 Jul 1992
         Last Updated on STN: 24 Jul 1992
Entered Medline: 13 Jul 1992
AB The secretion of pancreatic and gastrointestinal hormones in the basal state and after nutrient stimuli (50 g glucose, 50 g protein, or 30 g triglyceride administered on separate occasions) was assessed in ten
         previously type-1-diabetic patients after successful combined kidney and
         pancreas transplantation (systemic venous drainage). Fasting values were compared to matched non-diabetic kidney-transplanted patients and related to kidney function (endogenous creatinine clearance) and to the type and
        to titiney function (renogenous ceasinine treatance) and to the type and dosage of immunosuppressive medication. In the fasting state, only IR insulin concentrations were higher in pancreas-kidney-transplanted patients (by 88%, P = 0.001) than in the kidney graft recipients. There were significant inverse correlations of plasma C-peptide, GIP, and
         gastrin immunoreactivity to endogenous creatinine clearance (kidney function). In response to nutrients, insulin secretion (IR insulin,
       function). In response to nutrients, insulin secretion (IR insulin, C-peptide) was significantly stimulated by glucose, and - to a lesser degree - also by protein. Pancreatic glucagon was suppressed by glucose and stimulated by protein ingestion. GIP was raised after glucose and triglyceride more than after protein (P = 0.0003). GLP-l immunoreactivity was stimulated by all nutrients, with a tendency towards higher responses to protein and fat (P = 0.06). Gastrin was mainly raised by protein. In conclusion, the overall pattern of
```

Journal; Article; (JOURNAL ARTICLE)

DOCUMENT TYPE:

pancreatic and gastrointestinal hormone release is normal in patients after combined pancreas-kidney-transplantation, but there are some peculiarities due to (a) systemic venous drainage of the pancreas graft (elevated fasting IR insulin) and (b) impaired kidney function (negative correlation of fasting plasma values to endogenous creatinine clearance for C-peptide, GIP, and gastrin).(ABSTRACT TRUNCATED AT.250 WORDS) CT Check Tags: Female; Male Adult Blood Glucose: ME, metabolism Diabetes Mellitus, Type 1: SU, surgery Diabetic Nephropathies: BL, blood *Diabetic Nephropathies: BL, blood *Diabetic Nephropathies: SU, surgery *Gastrointestinal Hormones: BL, blood Humans

*Gastrointestinal Hormones: BL, blood
Humans
Kidney Function Tests
*Kidney Transplantation: PH, physiology
Middle Aged
*Pancreas Transplantation: PH, physiology
Pancreatic Function Tests
*Pancreatic Hormones: BL, blood
Research Support, Non-U.S. Gov't
CN 0 (Blood Glucose); 0 (Gastrointestinal Hormones); 0 (Pancreatic Hormones)